CHAPTER II

HISTORICAL

1. Alkaloids isolated from

a) *Uncaria* species and

b) other botanical sources containing *Uncaria* alkaloids.

Four tetracyclic oxindole alkaloids, isorhynchophylline, rhynchophylline, corynoxine and corynoxine B were reported to be present in the leaves of *Uncaria macrophylla* Wall. from Assam, Indo-China and China (Phillipson and Hemingway, 1973c).

Other alkaloids reported to be distributed both in genus *Uncaria* and in other genera are summarised below.

1.1 Pentacyclic heteroyohimbine alkaloids.

1.1.1 ajmalicine (δ-yohimbine, raubasine, py-tetrahydroserpentine)

a) -*Uncaria africana* G.Don. : leaf

-*U. africana* G.Don. var. *domatifera* Petit : leaf

-*U. bernaysii* F.v.Muell. : flower

-*U. orientalis* Guill. : leaf

(Phillipson *et al.*, 1978)

-*Catharanthus lanceus* (Boj. ex A. DC.) Pich. or *Vinca lancea* Boj. ex A. DC. or *Lochnera lancea* (Boj. ex A. DC.) K. Schum.

(Saxton, 1960; Farnsworth, 1972; Taylor and Farnsworth, 1975)

-*Catharanthus longifolius* (Pich.) Pich.

-*C. pusillus* (Murray) G.Don.

(Taylor and Farnsworth, 1975.)

-*C. roseus* (Linn.) G.Don. or *Vinca rosea* Linn. or *Lochnera rosea* (Linn.) Reichb.

(Saxton, 1960; Taylor and Farnsworth, 1975; Sarin *et al.*, 1977; Arens *et al.*, 1978.)

-*C. trichophyllus* (Baker) Pich.

(Rungsiyakul, 1973; Taylor and Farnsworth, 1975.)

-*Corynanthe yohombe* K.Schum. or *Pausinystalia yohimbe* Pierre.

(Robinson and Thomas, 1954; Saxton, 1960; Taylor and Farnsworth, 1975.)

-*Mitragyna javanica* Koord et Val.

(Shellard, 1971.)

-*M. javanica* var. *microphylla* Koord et Val.

(Shellard *et al.*, 1967a; Taylor and Farnsworth, 1975.)

-*M. parvifolia* (Roxb.) Korth.

(Shellard, 1971; Shellard and Houghton, 1972b.)

-*M. speciosa* Korth.

(Beckett *et al.*, 1966b; Trager *et al.*, 1968a; Shellard, 1971; Shellard *et al.*, 1978a, b.)

-*Picralima nitida* (Stapf.) Th. et H.Durand.

(Robinson and Thomas, 1954.)

-*Rauvolfia affinis* Muell.-Arg.

(Schlittler, 1965.)

-*Rauvolfia amsoniaefolia* A. DC.

(Rungsiyakul, 1973)

-*R. beddomei* Hook. f.

(Saxton, 1960; Schlittler, 1965)

-*R. caffra* Sond.

(Schlittler, 1965; Taylor and Farnsworth, 1975; Madati *et al.*, 1977)

-*R. canescens* Linn.

(Saxton, 1960; Schlittler, 1965; Taylor and Farnsworth, 1975)

-*R. chinensis* (Hance) Hemsl.

(Rungsiyakul, 1973; Taylor and Farnsworth, 1975)

-*R. cumminsii* Stapf.

(Iwu and Court, 1978b)

-*R. fruticosa* Burck.

(Schlittler, 1965)

-*R. heterophylla* Roem. et Schult.

(Saxton, 1960; Schlittler, 1965; Taylor and Farnsworth, 1975)

-*R. inebrians* K. Schum.

-*R. javanica* Koord et Val.

(Schlittler, 1965)

-*R. ligustrina* Roem. et Schult.

(Muller, 1957; Schlittler, 1965)

-*R. micrantha* Hook. f.

(Saxton, 1960; Schlittler, 1965; Taylor and Farnsworth, 1975)

-*Rauvolfia nitida* Jacq.

-*R. pentaphylla* Ducke.

-*R. rosea* K. Schum.

(Schlittler, 1965)

-*R. sellowii* Muell.-Arg.

(Hochstein, 1955; Saxton, 1960; Schlittler, 1965)

-*R. serpentina* Benth. ex Kurz.

(Marion, 1952; Saxton, 1960; Schlittler, 1965; Taylor and Farnsworth, 1975; Sarin *et al.*, 1977)

-*R. sumatrana* (Miq.) Jack

(Schlittler, 1965)

-*R. tetraphylla* Linn.

(Taylor and Farnsworth, 1975)

-*R. verticellata* (Lour.) Baill.

(Saxton, 1960; Schlittler, 1965; Taylor and Farnsworth, 1975)

-*R. viridis* (Muell.-Arg.) Guill.

(Schlittler, 1965)

-*R. vomitoria* Afzel.

(Marion, 1952; Schlittler, 1965; Taylor and Farnsworth, 1975)

-*R. yunnanensis* Tsiang.

-*Stemmadenia obovata* K. Schum.

(Taylor and Farnsworth, 1975)

-*Tonduzia longiflora* (A. DC.) Mgf.

-*Vinca erecta* Rgl. et Schmalh.

(Rungsiyakul, 1973)

-*Vinca rosea* Linn.

(Saxton, 1960)

1.1.2 3-isoajmalicine

a) -*Uncaria acida* (Hunt.) Roxb. var. *papuana* Val. : leaf

-*U. africana* G. Don. : leaf

-*U. africana* G. Don. var. *domatifera* Petit. : leaf

(Phillipson *et al.*,1978)

-*U. attenuata* Korth : leaf

(Phillipson and Hemingway, 1975b; Phillipson *et al.*,1978)

-*U. bernaysii* F.v.Muell. : leaf, flower

-*U. formosana* (Matsum.) Hayata : flower

-*U. homomalla* Miq. : leaf, stem

(Phillipson *et al.*,1978)

-*U. orientalis* Guill. : leaf

(Phillipson and Hemingway, 1975b; Phillipson *et al.*,1978)

-*U. rostrata* Pierre. ex Pitard. : leaf

(Phillipson *et al.*,1978)

-*U. salaccensis* Bakh. f. nom provis : leaf

(Wongseripipatana, 1979; Tantivatana *et al.*,1980)

-*U. sessilifructus* Roxb. : leaf

-*U. sterrophylla* Merr. et Perry : leaf

(Phillipson *et al.*,1978)

b) -*Mitragyna parvifolia* (Roxb.) Korth

(Shellard *et al.*,1968b, 1969b; Shellard, 1971, 1974; Shellard and Houghton, 1972b)

-*Mitragyna rotundifolia* (Roxb.) O.Kuntze

(Houghton and Shellard, 1974)

-*M. speciosa* Korth

(Shellard *et al.*,1978b)

1.1.3 tetrahydroalstonine

a) -*Uncaria africana* G. Don. : leaf

(Phillipson *et al.*,1978)

-*U. attenuata* Korth : leaf

(Phillipson *et al.*,1978; Supavita, 1979; Ponglux *et al.*,1980)

-*U. bernaysii* F.v.Muell. : leaf, stem, flower

(Phillipson and Hemingway, 1973a; Phillipson *et al.*,1978)

-*U. gambir* (Hunt.) Roxb. : leaf, stem

(Merlini *et al.*,1970; Phillipson *et al.*,1978)

b) -*Alstonia constricta* F.v.Muell.

(Saxton, 1965b; Beecham *et al.*,1968; Taylor and Farnsworth, 1975)

-*A. scholaris* R. Br.

(Dutta *et al.*,1976)

-*Catharanthus lanceus* (Boj. ex A. DC.) Pich.

(Saxton, 1965b; Farnsworth, 1972; Taylor and Farnsworth, 1975)

-*C. roseus* (Linn.) G. Don.

(Saxton, 1965b; Taylor and Farnsworth, 1975)

-*C. trichophyllus* (Baker) Pich.

(Taylor and Farnsworth, 1975)

-*Mitragyna parvifolia* (Roxb.) Korth

(Shellard, 1971; Shellard and Houghton, 1971, 1972b, 1974b)

-*Rauvolfia ligustrina* Roem. et Schult.

(Muller, 1957; Taylor and Farnsworth, 1975.)

-*R. obscura* K.Schum.

(Timmins and Court, 1976.)

-*R. sellowii* Muell.-Arg.

(Hochstein, 1955; Saxton, 1960; 1965b; Taylor and Farnsworth, 1975.)

-*R. vomitoria* Afzel.

(Taylor and Farnsworth, 1975; Sabri and Court, 1978.)

-*Vinca major* Linn.

(Rungsiyakul, 1973.)

1.1.4 akuammigine (3-isotetrahydroalstonine)

a) -*Uncaria attenuata* Korth : leaf

(Phillipson and Hemingway, 1975b; Phillipson *et al.*,1978.)

-*U. bernaysii* F.v.Muell. : leaf, stem, flower

(Phillipson and Hemingway, 1973a; Phillipson *et al.*,1978.)

-*U. gambir* (Hunt.) Roxb. : stem

(Merlini *et al.*,1972a.)

-*U. glabrescens* Merr. et Perry : leaf

-*U. orientalis* Guill : leaf

(Phillipson *et al.*,1978.)

-*U. rhynchophylla* Miq. : whole plant

(Aimi *et al.*,1977.)

-*U. rostrata* Pierre ex Pitard : leaf

-*U. sessilifructus* Roxb. : leaf

-*Uncaria sinensis* (Oliv.) Havil. : leaf, fruit, seed

(Phillipson *et al.*, 1978.)

b) -*Alstonia scholaris* R.Br.

(Boonchuay and Court, 1976.)

-*Mitragyna parvifolia* (Roxb.) Korth.

(Shellard *et al.*, 1968a, b, 1969a, b; Shellard, 1971; Shellard and Houghton, 1972b, 1974b; Shellard and Lala, 1977.)

-*M. speciosa* Korth.

(Shellard *et al.*, 1978b.)

-*Picralima nitida* (Stapf.) Th. et H.Durand.

(Henry, 1932; Robinson and Thomas, 1954; Saxton, 1960; Sarin *et al.*, 1977.)

1.1.5 4-R-akuammigine N-oxide and 4-S-akuammigine N-oxide

a) -*Uncaria gambir* (Hunt.) Roxb. : stem

(Chan, 1968; Merlini *et al.*, 1972b; Phillipson *et al.*, 1978.)

b) -*Mitragyna parvifolia* (Roxb.) Korth.

(Rungsiyakul, 1973; Shellard and Houghton, 1973, 1974b.)

1.1.6 19-epi-ajmalicine

a) -*Uncaria africana* G.Don. : leaf

(Phillipson *et al.*, 1978.)

1.1.7 19-epi-3-isoajmalicine

a) -*Uncaria africana* G.Don. var. *domatifera* Petit. : leaf

(Phillipson *et al.*, 1978.)

-*U. attenuata* Korth. : leaf

(Phillipson and Hemingway, 1975b; Phillipson *et al.*, 1978.)

-*Uncaria bulusanensis* Elm. : leaf

(Phillipson and Hemingway, 1975b.)

-*U. orientalis* Guill. : leaf

(Phillipson *et al.*, 1978.)

-*U. salaccensis* Bahk. f. nom provis : leaf

(Wongseripipatana, 1979; Tantivatana *et al.*, 1980.)

-*U. sessilifructus* Roxb. : leaf

(Phillipson *et al.*, 1978.)

1.1.8 raunitícine

a) -*Uncaria attenuata* Korth. : leaf

(Supavita, 1979; Ponglux *et al.*, 1980.)

b) -*Rauvolfia nitida* Jacq.

(Salkin *et al.*, 1961.)

1.1.9 14-hydroxy-3-isoraunitícine

a) -*Uncaria attenuata* Korth. : leaf

(Supavita, 1979; Ponglux *et al.*, 1980.)

1.2 Tetracyclic heteroyohimbine alkaloids

1.2.1 dihydrocorynantheine

a) -*Uncaria africana* G.Don. : leaf

-*U. attenuata* Korth. : leaf, stem bark, stem wood

(Phillipson and Hemingway, 1975b; Phillipson *et al.*, 1978.)

-*U. avenia* Val. : leaf

(Phillipson *et al.*, 1978.)

-*Uncaria bulusanensis* Elm. : leaf

(Phillipson and Hemingway, 1975b; Phillipson *et al.*, 1978.)

-*U. callophylla* Korth. : leaf

-*U. ferruginea* (Bl.) DC. : leaf, stem, flower

(Phillipson *et al.*, 1978.)

-*U. gambir* (Hunt.) Roxb. : leaf, stem

(Merlini *et al.*, 1970, 1972a; Phillipson *et al.*, 1978.)

-*U. guianensis* (Aubl.) Gmel. : leaf, stem, flower

-*U. jasminiflora* Hook f. : leaf

(Phillipson *et al.*, 1978.)

-*U. rhynchophylla* Miq. : stem, root, whole plant

(Aimi *et al.*, 1972, 1977; Phillipson *et al.*, 1978.)

-*U. sclerophylla* Havil. : leaf

(Phillipson *et al.*, 1978.)

-*U. tomentosa* DC. : leaf#, stem#, flower

(Hemingway and Phillipson, 1974; Phillipson *et al.*, 1978.)

-*U. valetoniana* Merr. et Perry : leaf

(Phillipson *et al.*, 1978.)

b) -*Cephalanthus occidentalis* Linn.

(Phillipson and Hemingway, 1974.)

-*Corynanthe yohimbe* K.Schum.

(Karrer *et al.*, 1952; Rungsiyakul, 1973.)

-*Mitragyna parvifolia* (Roxb.) Korth.

(Shellard *et al.*, 1969a, b; Shellard, 1971; Shellard and Houghton, 1972b.)

-*Pseudocinchona africana* Aug. Chev.

(Cu *et al.*, 1957; Rungsiyakul, 1973.)

1.2.2 hirsutine

a) -*Uncaria attenuata* Korth. : leaf, stem bark, stem wood

(Phillipson and Hemingway, 1975b; Phillipson *et al.*, 1978.)

-*U. guianensis* (Aubl.) Gmel. : leaf, stem, flower

-*U. kunstleri* King : leaf

(Phillipson *et al.*, 1978.)

-*U. rhynchophylla* Miq. : stem, root, whole plant

(Aimi *et al.*, 1972, 1977; Phillipson *et al.*, 1978.)

-*U. sessilifructus* Roxb. : leaf

(Phillipson *et al.*, 1978.)

-*U. tomentosa* DC. : leaf#, stem#, flower

(Hemingway and Phillipson, 1974; Phillipson *et al.*, 1978.)

-*U. valetoniana* Merr. et Perry : leaf

(Phillipson *et al.*, 1978.)

b) -*Cephalanthus occidentalis* Linn.

(Phillipson and Hemingway, 1974.)

-*Mitragyna hirsuta* Havil.

(Shellard *et al.*, 1967b; Shellard 1971; Phillipson *et al.*, 1973b; Houghton and Shellard, 1974.)

-*M. parvifolia* (Roxb.) Korth.

(Shellard *et al.*, 1969a, b; Shellard, 1971; Shellard and Houghton, 1972b; Shellard and Lala, 1977.)

-*M. rubrostipulata* (K.Schum.) Havil.

(Shellard and Lala, 1978.)

-*Mitragyna stipulosa* (DC.) O.Kuntze

(Houghton *et al.*, 1976.)

-*M. tubulosa* Havil.

(Rungsiyakul, 1973.)

1.2.3 corynantheine

a) -*Uncaria rhynchophylla* Miq. : stem, root, whole plant

(Aimi *et al.*, 1972, 1977; Phillipson *et al.*, 1978.)

b) -*Catharanthus roseus* (Linn.) G.Don.

(Taylor and Farnsworth, 1975.)

-*Corynanthe yohimbe* K.Schum.

(Karrer and Salomon, 1926; Marion, 1952.)

-*Mitragyna parvifolia* (Roxb.) Korth.

(Shellard and Houghton, 1972b.)

-*Pseudocinchona africana* Aug. Chev.

(Marion, 1952; Cu *et al.*, 1957.)

1.2.4 hirsuteine

a) -*Uncaria attenuata* Korth. : leaf, stem bark, stem wood

(Phillipson and Hemingway, 1975b; Phillipson *et al.*, 1978.)

-*U. guianensis* (Aubl.) Gmel. : leaf, stem, flower

(Hemingway and Phillipson, 1974; Phillipson *et al.*, 1978.)

-*U. rhynchophylla* Miq. : stem, root, whole plant

(Aimi *et al.*, 1972, 1977; Phillipson *et al.*, 1978.)

-*U. tomentosa* DC. : leaf, stem, flower

(Hemingway and Phillipson, 1974; Phillipson *et al.*, 1978.)

-*U. valetoniana* Merr. et Perry : leaf

(Phillipson *et al.*, 1978)

b) -*Mitragyna hirsuta* Havil.

(Phillipson *et al.*, 1973b)

-*M. parvifolia* (Roxb.) Korth.

(Shellard and Houghton, 1972a, b; Phillipson *et al.*, 1973b.)

-*M. rubrostipulata* (K.Schum.) Havil.

(Shellard and Lala, 1978.)

-*Pseudocinchona africana* Aug. Chev.

(Shellard and Houghton, 1972a.)

1.2.5 *epiallo*-corynantheine

a) -*Uncaria attenuata* Korth. : leaf

(Phillipson *et al.*, 1978.)

-*U. bulusanensis* Elm. : leaf

(Phillipson and Hemingway, 1975b; Phillipson *et al.*, 1978.)

1.2.6 gambirine

a) -*Uncaria callophylla* Korth. : leaf

(Phillipson and Hemingway, 1973d; Phillipson *et al.*, 1978.)

-*U. gambir* (Hunt.) Roxb. : gambier, leaf, stem

(Merlini *et al.*, 1967a, 1972a; Phillipson and Hemingway, 1973d; Phillipson *et al.*, 1978.)

-*U. jasminiflora* Hook f. : leaf

(Phillipson *et al.*, 1978.)

1.3 other indole alkaloids

1.3.1 β-carboline alkaloid : harmane (aribine, loturine, passiflorine)

a) -*Uncaria acida* (Hunt.) Roxb. : leaf

(Phillipson *et al.*,1978)

-*U. attenuata* Korth. : leaf

(Phillipson and Hemingway,1975b; Phillipson *et al.*,1978)

-*U. barbata* Merr. : leaf, fruit

-*U. borneensis* Havil. : leaf

-*U. callophylla* Korth. : leaf

(Phillipson *et al.*,1978)

-*U. canescens* Korth. : leaf, stem

(Phillipson and Hemingway,1975b; Phillipson *et al.*,1978)

-*U. ferrea* (Bl.)DC. : leaf, stem

(Phillipson *et al.*,1978)

-*U. orientalis* Guill. : leaf, stem

(Phillipson and Hemingway,1975b; Phillipson *et al.*,1978)

-*U. ovata* Hook.f. : leaf

(Phillipson *et al.*,1978)

b) -*Arariba rubra* Mart.

-*Calliygonum minimum* Lipski

-*Passiflora actinea* Hook.

-*P. alata* W.Ait.

-*P. bryonioides* H.B.K.

-*P. capsularis* Linn.

(Hesse,1964)

-*P. coerulea* Linn.

-*P. decrisneana* Hort.

(Lohdefink and Kating,1974)

-*P. edulis* Sims.

(Hesse,1964; Lohdefink and Kating,1974)

-*Passiflora eichleriana* Mast.

(Hesse, 1964.)

-*P. foetida* Linn.

(Lohdefink and Kating, 1974.)

-*P. incarnata* Linn.

(Hesse, 1964; Lohdefink and Kating, 1974.)

-*P. quadrangularis* Linn.

-*P. suberosa* Linn.

(Hesse, 1964.)

-*P. subpeltata* Orteg.

-*P. warmingii* Mart.

(Lohdefink and Kating, 1974.)

-*Symplocos racemosa* Roxb.

(Hesse, 1964.)

1.3.2 gambirtannine and its derivatives

1.3.2.1 gambirtannine

a) -*Uncaria gambir* (Hunt.) Roxb. : gambier

(Merlini *et al.*, 1967; Saxton, 1968; Phillipson and Hemingway, 1973d; Phillipson *et al.*, 1978.)

1.3.2.2 dihydrogambirtannine

a) -*Uncaria gambir* (Hunt.) Roxb. : gambier

(Merlini *et al.*, 1967; Saxton, 1968; Phillipson and Hemingway, 1973d; Phillipson *et al.*, 1978.)

1.3.2.3 oxogambirtannine

a) -*Uncaria gambir* (Hunt.) Roxb. : gambier

(Merlini *et al.*, 1967; Saxton, 1968; Phillipson and Hemingway, 1973d; Phillipson *et al.*, 1978.)

1.3.2.4 neo-oxygambirtannine

a) -*Uncaria gambir* (Hunt.) Roxb. : gambier

(Merlini *et al.*, 1967; Saxton, 1968; Phillipson and Hemingway, 1973d; Phillipson *et al.*, 1978.)

1.3.3 geissoschizine methyl ether

a) -*Uncaria rhynchophylla* Miq. : whole plant

(Aimi *et al.*, 1977.)

1.3.4 yohimbine alkaloids

1.3.4.1 yohimbine (quebrachamine, quebrachine)

a) -*Uncaria attenuata* Korth. : leaf, stem bark, stem wood

(Phillipson and Hemingway, 1975b; Phillipson *et al.*, 1978.)

b) -*Alchornea floribunda* Muell.-Arg.

(Hesse, 1964; Manske, 1965.)

-*Aspidosperma excelsum* Benth.

-*A. oblongum* A.DC.

(Taylor and Farnsworth, 1975.)

-*A. peroba* Saldanha da Gama

(Hesse, 1964.)

-*A. pyricollum* Muell.-Arg.

(Taylor and Farnsworth, 1975.)

-*Aspidosperma quebrachoblanco* Schlecht.

(Hesse, 1964; Manske, 1965; Taylor and Farnsworth, 1975)

-*Catharanthus lanceus* (Boj. ex A.DC.) Pich.

(Manske, 1965; Farnsworth, 1972; Taylor and Farnsworth, 1975.)

-*Corynanthe macroceras* K.Schum.

-*C. paniculata* Welw.

-*C. yohimbe* K.Schum.

-*Diplorrhynchus condylorcarpon* Pich.

(Hesse, 1964; Manske, 1965; Taylor and Farnsworth, 1975.)

-*Hunteria eburnea* Pich.

(Manske, 1965.)

-*Pausinystalia trillesii* Beille.

-*Pouteria* species

(Manske, 1965; Taylor and Farnsworth, 1975.)

-*Rauvolfia amsoniaefolia* A.DC.

-*R. canescens* Linn.

(Hesse, 1964; Taylor and Farnsworth, 1975.)

-*R. cumminsii* Stapf.

(Iwu and Court, 1978b.)

-*R. fruticosa* Burck.

-*R. heterophylla* Roem. et Schult.

(Hesse, 1964; Taylor and Farnsworth, 1975.)

-*R. ligustrina* Roem. et Schult.

(Hesse, 1964.)

-*R. mombasiana* Stapf.

(Iwu and Court, 1978a.)

-*Rauvolfia serpentina* (Linn.) Benth. ex Kurz.

-*R. sumatrana* (Miq.) Jack.

(Hesse, 1964; Taylor and Farnsworth, 1975.)

-*R. verticillata* (Lour.) Baill.

(Taylor and Farnsworth, 1975)

-*R. vomitoria* Afzel.

(Hesse, 1964.)

1.3.4.2 pseudo yohimbine

a) -*Uncaria attenuata* Korth. : leaf, stem bark, stem wood

(Phillipson and Hemingway, 1975b; Phillipson *et al.*, 1978.)

b) -*Catharanthus trichophyllus* (Baker) Pich.

(Cordell and Farnsworth, 1976.)

-*Corynanthe yohimbe* K.Schum.

(Hesse, 1964; Manske, 1965.)

-*Rauvolfia canescens* Linn.

-*R. tetraphylla* Linn.

(Hesse, 1964.)

1.3.5 pyridino-indolo-quinolizidinone alkaloids

1.3.5.1 angustine

a) -*Uncaria bernaysii* F.v.Muell. : flower

(Phillipson *et al.*, 1974, 1978.)

-*U. guianensis* (Aubl.) Gmel. : leaf, stem, flower

(Phillipson and Hemingway, 1974; Phillipson *et al.*, 1978.)

-*U. homomalla* Miq. : leaf, stem

(Phillipson *et al.*, 1974,1978.)

-*Uncaria parviflora* Ridl. : leaf, stem

(Phillipson *et al.*, 1978.)

-*U. rhynchophylla* Miq. : leaf

(Phillipson *et al.*, 1974, 1978.)

-*U. rhynchophylla* Miq. var. *kouteng* Yamazaki : leaf

-*U. tonkinensis* Havil. : leaf

(Phillipson *et al.*, 1978.)

b) -*Mitragyna javanica* Koord et Val.

-*M. parvifolia* (Roxb.) Korth

-*Nauclea coadunata* Roxb. ex J.E.Smith

-*Strychnos angolensis* Gilg.

(Phillipson *et al.*, 1974.)

-*S. angustiflora* Benth.

(Au *et al.*, 1973; Phillipson *et al.*, 1974.)

-*S. borneensis* Leenh.

(Phillipson *et al.*, 1974.)

-*S. camptoneura* Gilg. et Busse.

(Verpoorte *et al.*, 1975; Phillipson *et al.*, 1974.)

-*S. floribunda* Gilg.

-*S. ledermannii* Gilg. et Bened.

-*S. minor* Dennst.

-*S. odorata* A. Chev.

-*S. ovata* A.W.Hill.

-*S. potatorum* Linn. f.

-*S. samba* Duvign.

-*S. scheffleri* Gilg.

-*Strychnos trichoneura* Leeuwenberg

-*S. umbellata* (Lour.) Merr.

-*S. usambarensis* Gilg.

-*S. vanprukii* Craib.

-*S. xantha* Leeuwenberg

(Phillipson *et al.*, 1974.)

1.3.5.2 angustoline

a) -*Uncaria guianensis* (Aubl.) Gmel. : leaf, stem, flower

(Phillipson and Hemingway, 1974; Phillipson *et al.*, 1978.)

-*U. homomalla* Miq. : leaf, stem

(Phillipson *et al.*, 1974, 1978.)

-*U. parviflora* Ridl. : leaf, stem

(Phillipson *et al.*, 1978.)

-*U. rhynchophylla* Miq. : leaf

(Phillipson *et al.*, 1974, 1978.)

-*U. rhynchophylla* Miq. var. *kouteng* Yamazaki : leaf

-*U. tonkinensis* Havil. : leaf

(Phillipson *et al.*, 1978.)

b) -*Strychnos angustiflora* Benth.

(Au *et al.*, 1973; Phillipson *et al.*, 1974.)

-*S. borneensis* Leenh.

-*S. minor* Dennst.

-*S. odorata* A.Chev.

-*S. ovata* A.W.Hill

-*S. samba* Duvign

-*S. scheffleri* Gilg.

-*Strychnos trichoneura* Leeuwenberg

-*S. umbellata* (Lour.) Merr.

-*S. vanprukii* Craib.

-*S. xantha* Leeuwenberg

(Phillipson *et al.*, 1974.)

1.3.5.3 angustidine

a) -*Uncaria homomalla* Miq. : leaf, stem

(Phillipson *et al.*, 1974, 1978.)

-*U. parviflora* Ridl. : leaf, stem

(Phillipson *et al.*, 1978.)

-*U. rhynchophylla* Miq. : leaf

(Phillipson *et al.*, 1974, 1978.)

-*U. rhynchophylla* Miq. var. *kouteng* Yamazaki : leaf

-*U. tonkinensis* Havil. : leaf

(Phillipson *et al.*, 1978.)

b) -*Strychnos angolensis* Gilg.

(Phillipson *et al.*, 1974.)

-*S. angustiflora* Benth.

(Au *et al.*, 1973; Phillipson *et al.*, 1974.)

-*S. borneensis* Leenh

-*S. floribunda* Gilg.

-*S. minor* Dennst.

-*S. odorata* A.Chev.

-*S. ovata* A.W.Hill.

-*S. potatorum* Linn. f.

-*S. samba* Duvign.

-*Strychnos scheffleri* Gilg.

-*S. trichoneura* Leeuwenberg

-*S. umbellata* (Lour.) Merr.

-*S. usambarensis* Gilg.

-*S. vanprukii* Craib.

-*S. xantha* Leeuwenberg.

(Phillipson *et al.*, 1974.)

1.3.6 roxburghines

1.3.6.1 roxburghine A

a) -*Uncaria elliptica* R.Br. ex G.Don. : leaf

(Phillipson and Hemingway, 1973d; Phillipson *et al.*, 1978.)

-*U. gambir* (Hunt.) Roxb. : leaf

(Merlini *et al.*, 1970; Phillipson *et al.*, 1978.)

1.3.6.2 roxburghine B

a) -*Uncaria elliptica* R.Br. ex G.Don. : leaf

(Phillipson and Hemingway, 1973d; Phillipson *et al.*, 1978.)

-*U. gambir* (Hunt.) Roxb. : leaf, stem

(Merlini *et al.*, 1970, 1972b; Phillipson *et al.*, 1978.)

1.3.6.3 roxburghine C

a) -*Uncaria elliptica* R.Br. ex G.Don. : leaf

(Phillipson and Hemingway, 1973d; Phillipson *et al.*, 1978.)

-*U. gambir* (Hunt.) Roxb. : leaf

(Merlini *et al.*, 1970; Phillipson *et al.*, 1978.)

1.3.6.4 roxburghine D

a) -*Uncaria dasyoneura* Korth. : leaf

(Phillipson *et al.*, 1978.)

-*U. elliptica* R.Br. ex G.Don. : leaf

(Phillipson and Hemingway, 1973d; Phillipson *et al.*, 1978; Herath *et al.*, 1979.)

-*U. gambir* (Hunt.) Roxb. : leaf, stem

(Merlini *et al.*, 1970, 1972a; Phillipson *et al.*, 1978.)

-*U. rostrata* Pierre ex Pitard. : leaf

(Phillipson *et al.*, 1978.)

1.3.6.5 roxburghine E

a) -*Uncaria dasyoneura* Korth. : leaf

(Phillipson *et al.*, 1978.)

-*U. elliptica* R.Br. ex G.Don. : leaf

(Phillipson and Hemingway, 1973d; Phillipson *et al.*, 1978.)

-*U. gambir* (Hunt.) Roxb. : leaf, stem

(Merlini *et al.*, 1970; Phillipson *et al.*, 1978.)

1.3.6.6 roxburghine X

a) -*Uncaria elliptica* R.Br. ex G.Don. : plant

(Herath *et al.*, 1979.)

1.4 Pentacyclic Oxindole Alkaloids

1.4.1 isomitraphylline

a) -*Uncaria acida* (Hunt.) Roxb. var. *papuana* Val. : leaf,stem

-*U. africana* G.Don. : leaf

-*U. africana* G.Don. var. *domatifera* Petit. : leaf

-*U. africana* G.Don. var. *xerophila* Petit. : leaf

-*U. appendiculata* Benth. : leaf#

(Phillipson *et al.*, 1978)

-*U. attenuata* Korth. : leaf#

(Phillipson and Hemingway,1975b; Phillipson *et al.*, 1978)

-*U. bernaysii* F.v.Muell. : flower

-*U. callophylla* Korth. : leaf

(Phillipson *et al.*, 1978)

-*U. ferrea* (Bl.) DC. : leaf, flower

(Johns and Lamberton,1966; Phillipson *et al.*, 1978)

-*U. formosana* (Matsum.) Hayata. : leaf#,flower

-*U. guianensis* (Aubl.) Gmel. : leaf#

-*U. homomalla* Miq. : leaf,stem

-*U. hookeri* Val. : leaf

-*U. jasminiflora* Hook.f. : leaf

-*U. korrensis* Kanehira : leaf#

-*U. laevifolia* Elm. : leaf

-*U. laevigata* Wall. : leaf#

-*U. lancifolia* Hutch. : leaf

(Phillipson *et al.*, 1978)

-*Uncaria longiflora* (Poir.) Merr. : leaf #

(Phillipson and Hemingway, 1973b; Phillipson *et al.*,1978)

-*U. orientalis* Guill. : leaf #

(Phillipson and Hemingway, 1975b; Croquelois *et al.*,1977; Phillipson *et al.*,1978)

-*U. parviflora* Ridl. : leaf #, stem

-*U. perrottetii* (A. Rich.) Merr. : leaf #

-*U. pilosa* Roxb. : leaf #

-*U. pteropoda* Miq. : leaf #

(Phillipson *et al.*,1978)

-*U. quadrangularis* Geddes : leaf

(Tantivatana *et al.*,1979)

-*U. sessilifructus* Roxb. : leaf #

-*U. sterrophylla* Merr. et Perry : leaf

(Phillipson *et al.*,1978)

-*U. tomentosa* DC. : leaf #, stem #, flower

(Hemingway and Phillipson, 1974; Phillipson *et al.*,1978)

-*U. toppingii* Merr. : leaf #, stem, flower

-*U. velutina* Havil : leaf

(Phillipson *et al.*,1978)

b) -*Mitragyna hirsuta* Havil

(Shellard *et al.*,1967b; Shellard and Alam, 1968; Shellard, 1971; Bindra, 1973; Phillipson *et al.*,1973)

-*M. javanica* Koord et Val.

(Shellard and Alam, 1968; Shellard, 1971)

-*Mitragyna javanica* Koord et Val. var. *microphylla* Koord et Val.

(Shellard *et al.*,1967a; Bindra, 1973)

-*M. parvifolia* (Roxb.) Korth

(Shellard and Alam, 1968; Shellard *et al.*,1968b, 1969b; Shellard, 1971; Shellard and Houghton, 1972b; Bindra, 1973)

-*M. rotundifolia* (Roxb.) O.Kuntze

(Houghton and Shellard, 1974)

-*M. rubrostipulata* (K. Schum.) Havil

(Shellard and Lala, 1978)

-*M. speciosa* Korth

(Beckett *et al.*,1966a; Shellard and Alam, 1968; Trager *et al.*, 1968a; Shellard, 1971; Bindra, 1973; Shellard *et al.*,1978a, b)

-*M. tubulosa* Havil

(Rungsiyakul, 1973; Shellard and Rungsiyakul, 1973)

1.4.2 mitraphylline

a) -*Uncaria acida* (Hunt.) Roxb. var. *papuana* Val. : leaf, stem

-*U. africana* G. Don. : leaf #

-*U. africana* G. Don. var. *domatifera* Petit. : leaf

-*U. africana* G. Don. var. *xerophila* Petit. : leaf

-*U. appendiculata* Benth. : leaf

(Phillipson *et al.*,1978)

-*U. attenuata* Korth : leaf #

(Phillipson and Hemingway, 1975b; Phillipson *et al.*,1978)

-*U. bernaysii* F.v.Muell. : flower

-*U. callophylla* Korth : leaf

(Phillipson *et al.*,1978)

-*Uncaria elliptica* R. Br. ex G. Don. : plant

(Herath *et al.*,1979)

-*U. ferrea* (Bl.) DC. : leaf #, flower #

-*U. formosana* (Matsum.) Hayata : leaf #, flower, stem

(Phillipson *et al.*,1978)

-*U. gambir* (Hunt.) Roxb. : stem

(Chan, 1968; Phillipson *et al.*,1978)

-*U. guianensis* (Aubl.) Gmel. : leaf #, stem, flower

(Hemingway and Phillipson, 1974; Phillipson *et al.*,1978)

-*U. homomalla* Miq. : leaf

-*U. hookeri* Val. : leaf #

-*U. jasminiflora* Hook.f. : leaf

(Phillipson *et al.*,1978)

-*U. kawakamii* Havata : stem, bark, root

(Kariyone, 1958; Nozoye, 1958; Chan *et al.*,1966)

-*U. korrensis* Kanehira : leaf #

-*U. laevifolia* Elm. : leaf

-*U. laevigata* Wall. : leaf #

-*U. lancifolia* Hutch : leaf #

(Phillipson *et al.*,1978)

-*U. longiflora* (Poir.) Merr. : leaf

(Phillipson and Hemingway, 1973b; Phillipson *et al.*,1978)

-*U. orientalis* Guill. : leaf #

(Phillipson and Hemingway, 1975b; Croquelois *et al.*,1977;

Phillipson *et al.*,1978)

-*U. parviflora* Ridl. : leaf #, stem

-*Uncaria perrottetii* (A. Rich.) Merr. : leaf #

-*U. pilosa* Roxb. : leaf #

-*U. pteropoda* Miq. : leaf #

(Phillipson *et al.*,1978)

-*U. quadrangularis* Geddes : leaf

(Tantivatana *et al.*,1979)

-*U. salaccensis* Bakh. f. nom provis : leaf

(Wongseripipatana, 1979; Tantivatana *et al.*,1980)

-*U. sessilifructus* Roxb. : leaf #

-*U. sterrophylla* Merr. et Perry : leaf

(Phillipson *et al.*,1978)

-*U. tomentosa* DC. : leaf, stem, flower

(Hemingway and Phillipson, 1974; Phillipson *et al.*,1978)

-*U. toppingii* Merr. : leaf #, stem, flower

-*U. velutina* Havil : leaf

(Phillipson *et al.*,1978)

b) -*Catharanthus roseus* (Linn.) G. Don.

(Bindra, 1973; Taylor and Farnsworth, 1975)

-*Mitragyna hirsuta* Havil

(Shellard *et al.*,1967b; Shellard and Alam, 1968; Shellard, 1971; Bindra, 1973; Phillipson *et al.*,1973b)

-*M. javanica* Koord et Val.

(Shellard and Alam, 1968; Shellard, 1971)

-*M. javanica* Koord et Val. var. *microphylla* Koord et Val.

(Shellard *et al.*,1967a; Bindra, 1973)

-*Mitragyna parvifolia* (Roxb.) Korth

(Shellard and Alam, 1968; Shellard *et al.*,1968b, 1969b; Shellard, 1971; Shellard and Houghton, 1972b; Bindra, 1973)

-*M. rotundifolia* (Roxb.) O.Kuntze

(Shellard and Phillipson, 1964a; Houghton and Shellard, 1974)

-*M. rubrostipulata* (K.Schum.) Havil

(Badger *et al.*,1950; Shellard and Lala, 1978)

-*M. speciosa* Korth

(Shellard and Phillipson, 1964a; Beckett *et al.*,1966a; Shellard and Alam, 1968; Trager *et al.*,1968a; Shellard, 1971; Bindra, 1973; Shellard *et al.*,1978a, b)

-*M. stipulosa* (DC.) O.Kuntze

(Saxton, 1960; Beckett *et al.*,1963a; Shellard and Alam, 1968; Shellard and Sarpong, 1970; Shellard, 1971; Houghton *et al.*,1976)

-*M. tubulosa* Havil

(Rungsiyakul, 1973; Shellard and Rungsiyakul, 1973)

1.4.3 isopteropodine (uncarine E)

a) -*Uncaria appendiculata* Benth. : leaf #, stem #

(Phillipson *et al.*,1978)

-*U. bernaysii* F.v.Muell. : leaf #, stem #, hook #, flower #

(Johns and Lamberton, 1966; Beecham *et al.*,1968; Phillipson and Hemingway, 1973a, b; Phillipson *et al.*,1978)

-*U. brevicarpa* Elm. : leaf #

-*U. donisii* Petit. : leaf

(Phillipson *et al.*,1978)

-*Uncaria ferrea* (Bl.) DC. : leaf#, stem#, flower

(Beecham *et al.*, 1968: Phillipson *et al.*, 1978)

-*U. florida* Vidal. : leaf

(Aimi *et al.*,1972; Phillipson *et al.*,1978)

-*U. glabrata* (Bl.) DC. : leaf#

-*U. glabrescens* Merr.et Perry : leaf#

(Phillipson *et al.*,1978)

-*U.homomalla* Miq. : leaf#, stem#

(Ponglux *et al.*,1977; Phillipson *et al.*,1978)

-*U. hookeri* Val. : leaf

-*U. kawakamii* Havata : leaf#

-*U. korrensis* Kanehira : leaf#

-*U. laevifolia* Elm. : leaf

-*U. laevigata* Wall. : leaf

-*U. lanosa* Wall. : leaf#

-*U. lobbii* Hook.f. : leaf

(Phillipson *et al.*,1978)

-*U. longiflora* (Poir.) Merr. : leaf#

(Phillipson and Hemingway,1973b; Phillipson *et al.*,1978)

-*U. orientalis* Guill. : leaf#, flower

(Phillipson and Hemingway,1975b; Croquelois *et al.*,1977;

Phillipson *et al.*,1978)

-*U. parviflora* Ridl. : leaf

-*U. perrottetii* (A.Rich.) Merr. : leaf

-*U. philippinensis* Elm. : leaf

-*Uncaria pilosa* Roxb. : leaf #

(Phillipson *et al.*,1978)

-*U. pteropoda* Miq. : leaf #, stem, stem bark, root

(Chan *et al.*,1966; Yeoh *et al.*,1966; Phillipson *et al.*,1978)

-*U. quadrangularis* Geddes : stem bark

(Tantivatana *et al.*,1979)

-*U. roxburghiana* Korth : leaf #, stem #

-*U. setiloba* Benth. : leaf #, stem #

-*U. sinensis* (Oliv.) Havil : leaf #, fruit #, seed #

-*U. sterrophylla* Merr. et Perry : leaf, stem, stem bark

-*U. toppingii* Merr. : leaf #, stem, flower

(Phillipson *et al.*,1978)

-*U. velutina* Havil : leaf #

(Phillipson and Hemingway, 1975b; Phillipson *et al.*,1978)

b) -*Mitragyna parvifolia* (Roxb.) Korth

(Shellard and Alam, 1968; Shellard *et al.*,1968a, b, 1969a, b; Shellard, 1971; Bindra, 1973; Shellard and Houghton, 1972b, 1974b; Shellard and Lala, 1977)

1.4.4 pteropodine (uncarine C)

a) -*Uncaria appendiculata* Benth. : leaf #, stem #

(Phillipson *et al.*,1978)

-*U. bernaysii* F.v.Muell. : leaf #, stem #, hook #, flower #

(Johns and Lamberton, 1966; Beecham *et al.*,1968; Phillipson and Hemingway, 1973a, b; Phillipson *et al.*,1978)

-*U. brevicarpa* Elm. : leaf #

-*Uncaria donisii* Petit. : leaf#

(Phillipson *et al.*,1978)

-*U. ferrea* (Bl.) DC. : leaf#, stem#, flower,fruit, seed

(Johns and Lamberton,1966; Beecham *et al.*,1968; Phillipson *et al.*,1978)

-*U. florida* Vidal. : leaf

(Aimi *et al.*,1972; Phillipson *et al.*,1978)

-*U. glabrata* (Bl.) DC. : leaf#

-*U. glabrescens* Merr.et Perry : leaf#

(Phillipson *et al.*,1978)

-*U. homomalla* Miq. : leaf#, stem#

(Ponglux *et al.*, 1977; Phillipson *et al.*, 1978)

-*U. hookeri* Val. : leaf

-*U. kawakamii* Havata : leaf#

-*U. korrensis* Kanehira : leaf#

-*U. laevifolia* Elm. : leaf

-*U. lanosa* Wall. : leaf#

-*U. lobbii* Hook.f. : leaf

(Phillipson *et al.*,1978)

-*U. longiflora* (Poir.) Merr. : leaf#

(Phillipson and Hemingway, 1973b; Phillipson *et al.*,1978)

-*U. orientalis* Guill. : leaf#, flower

(Phillipson and Hemingway, 1975b; Phillipson *et al.*,1978)

-*U. parviflora* Ridl. : leaf

-*U. perrottetii* (A.Rich.) Merr. : leaf

-*U. philippinensis* Elm. : leaf#

-*Uncaria pilosa* Roxb. : leaf #

(Phillipson *et al.*,1978)

-*U. pteropoda* Miq. : leaf #, stem, stem bark, root

(Chan *et al.*,1966; Yeoh *et al.*,1966; Phillipson *et al.*,1978)

-*U. quadrangularis* Geddes : stem bark

(Tantivatana *et al.*,1979)

-*U. roxburghiana* Korth : leaf #, stem

-*U. setiloba* Benth. : leaf #, stem #

-*U. sinensis* (Oliv.) Havil : leaf #, fruit #, seed #

-*U. sterrophylla* Merr. et Perry : leaf, stem, stem bark

-*U. toppingii* Merr. : leaf, flower

(Phillipson *et al.*,1978)

-*U. velutina* Havil : leaf #

(Phillipson and Hemingway, 1975b; Phillipson *et al.*,1978)

b) -*Mitragyna parvifolia* (Roxb.) Korth

(Shellard and Alam, 1968; Shellard *et al.*,1968a, b, 1969a, b; Shellard, 1971; Bindra, 1973; Shellard and Houghton, 1972b, 1974b; Shellard and Lala, 1977)

1.4.5 speciophylline (uncarine D)

a) -*Uncaria acida* (Hunt.) Roxb. var. *papuana* Val. : leaf, stem

-*U. appendiculata* Benth. : leaf #, stem #

(Phillipson *et al.*,1978)

-*U. attenuata* Korth : leaf

(Phillipson and Hemingway, 1975b; Phillipson *et al.*,1978)

-*U. bernaysii* F.v.Muell. : leaf #, stem #, hook #, flower #

(Johns and Lamberton, 1966; Beecham *et al.*,1968; Phillipson and

Hemingway, 1973a, b; Phillipson *et al.*, 1978)

-*Uncaria brevicarpa* Elm. : leaf #, fruit, seed

-*U. donisii* Petit. : leaf #

(Phillipson *et al.*, 1978)

-*U. ferrea* (Bl.) DC. : leaf #, flower #, stem #, fruit, seed

(Johns and Lamberton, 1966; Beecham *et al.*, 1968; Phillipson *et al.*, 1978)

-*U. florida* Vidal. : leaf

-*U. glabrata* (Bl.) DC. : leaf #, stem

-*U. glabrescens* Merr. et Perry : leaf #

(Phillipson *et al.*, 1978)

-*U. homomalla* Miq. : leaf #, stem #

(Ponglux *et al.*, 1977; Phillipson *et al.*, 1978)

-*U. hookeri* Val. : leaf

-*U. kawakamii* Havata : leaf #

-*U. korrensis* Kanehira : leaf

-*U. laevigata* Wall. : leaf

-*U. lanosa* Wall. : leaf #

-*U. lobbii* Hook. f. : leaf #

(Phillipson *et al.*, 1978)

-*U. longiflora* (Poir.) Merr. : leaf #

(Phillipson and Hemingway, 1973b; Phillipson *et al.*, 1978)

-*U. orientalis* Guill. : leaf #, flower

(Phillipson and Hemingway, 1975b; Phillipson *et al.*, 1978)

-*U. parviflora* Ridl. : leaf

-*U. perrottetii* (A. Rich.) Merr. : leaf

-*Uncaria philippinensis* Elm. : leaf #

-*U. pilosa* Roxb. : leaf #

-*U. pteropoda* Miq. : leaf #

-*U. roxburghiana* Korth : leaf #, stem #

-*U. setiloba* Benth. : leaf, stem

-*U. sinensis* (Oliv.) Havil : leaf #, fruit #, seed

-*U. sterrophylla* Merr. et Perry : leaf #, stem, stem bark

-*U. toppingii* Merr. : Leaf #, flower #

(Phillipson *et al.*,1978)

-*U. velutina* Havil : leaf #

(Phillipson and Hemingway, 1975b; Phillipson *et al.*,1978)

b) -*Mitragyna inermis* (Willd.) O.Kuntze

(Shellard and Sarpong, 1969, 1970; Shellard, 1971; Bindra, 1973)

-*M. parvifolia* (Roxb.) Korth

(Shellard and Alam, 1968; Shellard *et al.*,1968a, b, 1969b; Shellard, 1971; Bindra, 1973; Shellard and Houghton, 1972b, 1974b; Rungsiyakul, 1973; Shellard and Lala, 1977)

-*M. speciosa* Korth

(Beckett *et al.*,1966a; Johns and Lamberton, 1966; Shellard and Alam, 1968; Shellard *et al.*,1968a, 1978a; Shellard, 1971; Bindra, Bindra, 1973)

1.4.6 uncarine F

a) -*Uncaria appendiculata* Benth. : leaf #, stem #

(Phillipson *et al.*,1978)

-*U. bernaysii* F.v.Muell. : leaf #, stem #, hook #, flower #

(Beecham *et al.*,1968; Phillipson and Hemingway, 1973a; Phillipson *et al.*,1978)

-*Uncaria brevicarpa* Elm. : leaf

-*U. donisii* Petit. : leaf#

(Phillipson *et al.*, 1978)

-*U. ferrea* (Bl.) DC. : leaf#, stem, flower, fruit, seed

(Beecham *et al.*, 1968; Phillipson *et al.*, 1978)

-*U. glabrata* (Bl.) DC. : leaf#

-*U. glabrescens* Merr. et Perry : leaf#

(Phillipson *et al.*, 1978)

-*U. homomalla* Miq. : leaf#, stem#

(Ponglux *et al.*, 1977; Phillipson *et al.*, 1978)

-*U. hookeri* Val. : leaf

-*U. kawakamii* Havata : leaf#

-*U. korrensis* Kanehira : leaf#

-*U. laevifolia* Elm. : leaf

-*U. lanosa* Wall. : leaf#

-*U. lobbii* Hook.f. : leaf

(Phillipson *et al.*, 1978)

-*U. longiflora* (Poir.) Merr. : leaf#

(Phillipson and Hemingway, 1973b; Phillipson *et al.*, 1978)

-*U. orientalis* Guill. : leaf#

(Phillipson and Hemingway, 1975b; Phillipson *et al.*, 1978)

-*U. parviflora* Ridl. : leaf

-*U. perrottetii* (A.Rich.) Merr. : leaf

-*U. philippinensis* Elm. : leaf#

-*U. pilosa* Roxb. : leaf

-*U. pteropoda* Miq. : leaf#

-*Uncaria roxburghiana* Korth : leaf, stem

-*U. sessilifructus* Roxb. : leaf

-*U. setiloba* Benth. : leaf #, stem #

-*U. sinensis* (Oliv.) Havil : leaf #, fruit #, seed #

-*U. sterrophylla* Merr. et Perry : leaf, stem bark

-*U. toppingii* Merr. : leaf, flower

(Phillipson *et al.*,1978)

-*U. velutina* Havil : leaf

(Phillipson and Hemingway, 1975b; Phillipson *et al.*,1978)

b) -*Mitragyna inermis* (Willd.) O.Kuntze

(Shellard and Sarpong, 1969, 1970; Shellard, 1971; Bindra, 1973)

-*M. parvifolia* (Roxb.) Korth

(Shellard and Alam, 1968; Shellard *et al.*,1968a, b, 1969b; Shellard, 1971; Shellard and Houghton, 1972b, 1974b; Bindra, 1973; Rungsiyakul, 1973; Shellard and Lala, 1977)

1.4.7 uncarine A (isoformosanine)

a) -*Uncaria attenuata* Korth : leaf

(Phillipson and Hemingway, 1975b; Phillipson *et al.*,1978)

-*U. formosana* (Matsum.) Hayata : leaf, flower

(Phillipson *et al.*,1978)

-*U. kawakamii* Havata : stem, bark, root

(Kariyone, 1958; Saxton, 1960; Chan *et al.*,1966; Yeoh *et al.*, 1966)

-*U. laevigata* Wall. : leaf

-*U. sessilifructus* Roxb. : leaf

(Phillipson *et al.*,1978)

1.4.8 uncarine B (formosanine)

a) -*Uncaria attenuata* Korth : leaf

(Phillipson and Hemingway, 1975b; Phillipson *et al.*, 1978)

-*U. elliptica* R. Br. ex G. Don. : plant

(Herath *et al.*, 1979)

-*U. formosana* (Matsum.) Hayata : leaf, flower, stem

(Saxton, 1960; Phillipson *et al.*, 1978)

-*U. kawakamii* Hayata : stem, bark, root

(Nozoye, 1958; Saxton, 1960; Chan *et al.*, 1966; Yeoh *et al.*, 1966)

-*U. laevigata* Wall. : leaf

(Phillipson *et al.*, 1978)

-*U. salaccensis* Bakh. f. nom provis : leaf

(Wongseripipatana, 1979; Tantivatana *et al.*, 1980)

-*U. sessilifructus* Roxb. : leaf

(Phillipson *et al.*, 1978)

1.4.9 gambirdine and isogambirdine

a) -*Uncaria gambir* (Hunt.) Roxb. : stem

(Chan, 1968; Merlini *et al.*, 1972b; Phillipson *et al.*, 1978)

1.5 Tetracyclic Oxindole Alkaloids

1.5.1 isorhynchophylline

a) -*Uncaria acida* (Hunt.) Roxb. : leaf

-*U. acida* (Hunt.) Roxb. var. *papuana* Val. : leaf #, stem

-*U. africana* G. Don. : leaf

-*U. angolensis* Welw. : leaf #

(Phillipson *et al.*, 1978)

-*Uncaria attenuata* Korth : leaf #, stem bark #, stem wood #

(Phillipson and Hemingway, 1975b; Phillipson *et al.*, 1978)

-*U. avenia* Val. : leaf, stem

-*U. bernaysii* F.v.Muell. forma *inermis* K. Schum. : leaf #

-*U. bernaysioides* Merr. et Perry : leaf #

-*U. callophylla* Korth : leaf

-*U. cordata* (Lour.) Merr. : leaf, stem, flower

(Phillipson *et al.*, 1978)

-*U. gambir* (Hunt.) Roxb. : leaf

(Merlini *et al.*, 1970, 1972a; Phillipson *et al.*, 1978)

-*U. guianensis* (Aubl.) Gmel. : leaf #, stem, flower

(Hemingway and Phillipson, 1974; Phillipson *et al.*, 1978)

-*U. halleri* Korth : leaf

-*U. jasminiflora* Hook. f. : leaf

-*U. kunstleri* King : leaf #

-*U. longiflora* (Poir.) Merr. : leaf #, stem #

(Phillipson *et al.*, 1978)

-*U. macrophylla* Wall. : leaf #, stem #

(Phillipson and Hemingway, 1973c; Phillipson *et al.*, 1978)

-*U. orientalis* Guill. : plant

(Croquelois *et al.*, 1977)

-*U. pedicellata* Roxb. : leaf

-*U. pteropoda* Miq. : leaf

(Phillipson *et al.*, 1978)

-*U. rhynchophylla* Miq. : leaf, stem, root, hook

(Saxton, 1965a; Aimi *et al.*, 1972, 1977; Phillipson *et al.*, 1978)

-*Uncaria rhynchophylla* Miq. var. *kouteng* Yamazaki : leaf[#]

-*U. sclerophylla* Havil. : leaf

-*U. sessilifructus* Roxb. : leaf

-*U. sterrophylla* Merr. et Perry : leaf, stem bark, stem wood

-*U. talbotii* Wernh. : leaf, flower

(Phillipson *et al.*, 1978.)

-*U. tomentosa* DC. : leaf[#], stem[#], flower[#]

(Hemingway and Phillipson, 1974; Phillipson *et al.*, 1978.)

b) -[#]*Cephalanthus occidentalis* Linn.

(Phillipson and Hemingway, 1974.)

-*Mitragyna ciliata* Aubrev. et Pellegr.

(Beckett *et al.*, 1963b; Shellard and Phillipson, 1964a; Shellard and Alam, 1968; Shellard and Sarpong 1970; Shellard, 1971.)

-*M. hirsuta* Havil.

(Shellard *et al.*, 1967b; Shellard and Alam, 1968; Shellard, 1971; Bindra, 1973; Phillipson *et al.*, 1973.)

-[#]*M. inermis* (Willd.) O.Kuntze

(Shellard and Alam, 1968; Shellard and Sarpong 1969, 1970; Shellard, 1971; Shellard *et al.*, 1971; Bindra, 1973; Shellard *et al.*, 1978a.)

-*M. parvifolia* (Roxb.) Korth.

(Shellard and Phillipson, 1964b; Shellard and Alam, 1968; Shellard *et al.*, 1968b, 1969a, b; Shellard, 1971; Shellard and Houghton, 1972b; Shellard and Lala, 1977.)

-[#]*Mitragyna rotundifolia* (Roxb.) O.Kuntze

(Shellard and Phillipson, 1964a; Shellard and Alam, 1968; Shellard, 1971; Shellard *et al.*, 1971; Houghton and Shellard, 1974.)

-*M. rubrostipulata* (K.Schum.) Havil.

(Beckett *et al.*, 1963a; Shellard and Phillipson, 1964a; Shellard and Lala, 1978.)

-*M. speciosa* Korth.

(Shellard and Alam, 1968; Shellard *et al.*, 1978a, b.)

-*M. stipulosa* (DC.) O.Kuntze.

(Beckett *et al.*, 1963a; Shellard and Phillipson, 1964a; Shellard and Alam, 1968; Shellard and Sarpong, 1970; Shellard, 1971; Houghton *et al.*, 1976.)

-*M. tubulosa* Havil.

(Rungsiyakul, 1973; Shellard and Rungsiyakul, 1973.)

1.5.2 rhynchophylline (mitrinermine)

a) -*Uncaria acida* (Hunt.) Roxb. : leaf

-*U. acida* (Hunt.) Roxb. var. *papuana* Val. : leaf[#], stem

-*U. africana* G.Don. : leaf

-*U. angolensis* Welw. : leaf[#]

(Phillipson *et al.*, 1978.)

-*U. attenuata* Korth. : leaf[#], stem bark[#], Stem wood[#]

(Phillipson and Hemingway, 1975b; Phillipson *et al.*, 1978.)

-*U. avenia* Val. : leaf

-*U. bernaysii* F.v. Muell. forma *inermis* K.Schum. : leaf[#]

-*Uncaria bernaysioides* Merr. et Perry : leaf#

(Phillipson *et al.*, 1978.)

-*U. bulusanensis* Elm. : leaf

(Phillipson and Hemingway, 1975b.)

-*U. callophylla* Korth. : leaf

-*U. cordata* (Lour.) Merr. : leaf, stem, flower

(Phillipson *et al.*, 1978.)

-*U. gambir* (Hunt.) Roxb. : leaf

(Merlini *et al.*, 1970, 1972a; Phillipson *et al.*, 1978.)

-*U. guianensis* (Aubl.) Gmel. : leaf#, stem#, flower#

(Phillipson and Hemingway, 1974; Phillipson *et al.*, 1978.)

-*U. halleri* Korth. : leaf

-*U. jasminiflora* Hook.f. : leaf

-*U. kunstleri* King. : leaf#

-*U. longiflora* (Poir.) Merr. : leaf, stem#

(Phillipson *et al.*, 1978.)

-*U. macrophylla* Wall. : leaf#, stem#

(Phillipson and Hemingway, 1973c; Phillipson *et al.*, 1978.)

-*U. orientalis* Guill.

(Croquelois *et al.*, 1977.)

-*U. pedicellata* Roxb. : leaf

-*U. pteropoda* Miq. : leaf

(Phillipson *et al.*, 1978.)

-*U. rhynchophylla* Miq. : leaf#, stem#, root, hook

(Saxton, 1965a; Aimi *et al.*, 1972, 1977; Phillipson *et al.*, 1978.)

-*U. rhynchophylla* Miq. var. *kouteng* Yamazaki : leaf

-*U. sclerophylla* Havil. : leaf

-*U. sessilifructus* Roxb. : leaf

-*U. sterrophylla* Merr. et Perry : leaf, stem bark, stem wood

-*U. talbotii* Wernh. : leaf, flower

(Phillipson *et al.*, 1978.)

-*U. tomentosa* DC. : leaf#, stem#, flower#

(Hemingway and Phillipson, 1974; Phillipson *et al.*, 1978.)

b) #*Cephalanthus occidentalis* Linn.

(Phillipson and Hemingway, 1974.)

-*Crossopteryx kotschyana* Fenzl.

(Saxton, 1965a)

-*Mitragyna ciliata* Aubrev. et Pellegr.

(Beckett *et al.*, 1963a, b; Saxton, 1965a; Shellard and Alam, 1968; Shellard and Sarpong, 1970; Shellard, 1971.)

-*M. hirsuta* Havil.

(Shellard *et al.*, 1967b; Shellard and Alam, 1968; Shellard, 1971; Bindra, 1973; Phillipson *et al.*, 1973; Houghton and Shellard, 1974.)

-#*M. inermis* (Willd.) O.Kuntze

(Beckett *et al.*, 1963a; Saxton, 1965a; Shellard and Alam, 1968; Shellard and Sarpong, 1969, 1970; Shellard, 1971; Bindra, 1973; Shellard *et al.*, 1971, 1978a.)

-*M. parvifolia* (Roxb.) Korth.

(Shellard and Phillipson, 1964b; Shellard and Alam, 1968; Shellard *et al.*, 1968b, 1969a, b; Shellard, 1971; Shellard and

Houghton, 1972b; Shellard and Lala, 1977.)

-#*Mitragyna rotundifolia* (Roxb.) O.Kuntze

(Shellard and Phillipson, 1964a; Saxton, 1965a; Shellard and Alam, 1968; Shellard, 1971; Shellard *et al.*, 1971; Houghton and Shellard, 1974.)

-#*M. rubrostipulata* (K.Schum.) Havil.

(Hendrickson and Sims, 1963; Shellard and Lala, 1978.)

-*M. speciosa* Korth.

(Hendrickson and Sims, 1963; Shellard and Phillipson, 1964a; Beckett *et al.*, 1965b; Shellard and Alam, 1968; Trager *et al.*, 1968a; Bindra, 1973; Shellard *et al.*, 1978a, b.)

-*M. stipulosa* (DC.) O.Kuntze

(Beckett *et al.*, 1963a; Saxton, 1965a; Shellard and Alam, 1968; Shellard and Sarpong, 1970; Shellard, 1971; Houghton *et al.*, 1976.)

-*M. tubulosa* Havil.

(Rungsiyakul, 1973; Shellard and Rungsiyakul, 1973.)

1.5.3 corynoxine

a) -*Uncaria kunstleri* King : leaf

-*U. longiflora* (Poir.) Merr. : leaf

(Phillipson *et al.*, 1978.)

-*U. macrophylla* Wall. : leaf, stem

(Phillipson and Hemingway, 1973c; Phillipson *et al.*, 1978.)

-*U. pedicellata* Roxb. : leaf

-*U. sessilifructus* Roxb. : leaf

(Phillipson *et al.*, 1978.)

b) -*Corynanthe yohimbe* K.Schum.

(Cu *et al.*,1957)

-*Mitragyna speciosa* Korth.

(Shellard *et al.*,1978a)

-*Pseudocinchona africana* Aug.Chev.

(Cu *et al.*,1957; Phillipson and Hemingway,1973c)

1.5.4 corynoxine B

a) -*Uncaria attenuata* Korth. : leaf

-*U. bulusanensis* Elm. : leaf

(Phillipson and Hemingway,1975b; Phillipson *et al.*,1978)

-*U. kunstleri* King : leaf

-*U. longiflora* (Poir.)Merr.

(Phillipson *et al.*,1978)

-*U. macrophylla* Wall. : leaf, stem

(Phillipson and Hemingway,1973c; Phillipson *et al.*,1978)

-*U. pedicellata* Roxb. : leaf

-*U. sessilifructus* Roxb. : leaf

(Phillipson *et al.*,1978)

b) -*Mitragyna speciosa* Korth.

(Shellard *et al.*,1978a)

1.5.5 isocorynoxeine

a) -*Uncaria attenuata* Korth. : leaf, Stem bark, stem wood

(Phillipson and Hemingway,1975b; Phillipson *et al.*,1978)

-*U. longiflora* (Poir.)Merr. : leaf

-*U. pteropoda* Miq. : leaf

(Phillipson *et al.*,1978)

-*Uncaria rhynchophylla* Miq. : leaf, stem, root, whole plant

(Aimi *et al.*,1972, 1977; Phillipson *et al.*,1978)

-*U. rhynchophylla* Miq. var. *kouteng* Yamazaki : leaf

(Phillipson *et al.*,1978)

b) -*Mitragyna rotundifolia* (Roxb.) O.Kuntze

(Houghton and Shellard, 1974)

1.5.6 corynoxeine

a) -*Uncaria acida* (Hunt.) Roxb. var. *papuana* Val. : leaf

(Phillipson *et al.*,1978)

-*U. attenuata* Korth : leaf, stem bark, stem wood

(Phillipson and Hemingway, 1975b; Phillipson *et al.*,1978)

-*U. longiflora* (Poir.) Merr. : leaf

-*U. pteropoda* Miq. : leaf

(Phillipson *et al.*,1978)

-*U. rhynchophylla* Miq. : leaf, stem, root, whole plant

(Aimi *et al.*,1972, 1977; Phillipson *et al.*,1978)

-*U. rhynchophylla* Miq. var. *kouteng* Yamazaki : leaf

(Phillipson *et al.*,1978)

b) -*Corynanthe yohimbe* K. Schum.

(Cu *et al.*,1957)

-*Mitragyna hirsuta* Havil

(Houghton and Shellard, 1974)

-*M. parvifolia* (Roxb.) Korth

(Shellard and Houghton, 1972a, b; Shellard *et al.*,1978b)

-*M. rotundifolia* (Roxb.) O.Kuntze

(Shellard *et al.*,1967b; Houghton and Shellard, 1974)

-*Mitragyna speciosa* Korth

(Shellard *et al.*, 1978a)

-*M. stipulosa* (DC.) O.Kuntze

(Houghton *et al.*, 1976)

-*Pseudocinchona africana* Aug. Chev.

(Cu *et al.*, 1957; Shellard and Houghton, 1972a)

1.5.7 rotundifoline (stipulatine)

a) -*Uncaria attenuata* Korth : leaf

-*U. bulusanensis* Elm. : leaf

(Phillipson and Hemingway, 1975b; Phillipson *et al.*, 1978)

-*U. gambir* (Hunt.) Roxb. : leaf

(Merlini *et al.*, 1970, 1972a; Phillipson *et al.*, 1978)

-*U. tomentosa* DC. : leaf, stem, flower

(Hemingway and Phillipson, 1974; Phillipson *et al.*, 1978)

b) -*Mitragyna ciliata* Aubrev et Pellegr.

(Saxton, 1960; Beckett *et al.*, 1963b; Shellard and Alam, 1968; Shellard and Sarpong, 1970; Shellard, 1971)

-*M. inermis* (Willd.) O.Kuntze

(Shellard and Alam, 1968; Shellard and Sarpong, 1969, 1970; Shellard, 1971; Bindra, 1973)

-*M. parvifolia* (Roxb.) Korth

(Shellard and Phillipson, 1964b; Shellard *et al.*, 1968b; Shellard and Alam, 1968; Shellard, 1971; Hemingway *et al.*, 1975)

-*M. rotundifolia* (Roxb.) O.Kuntze

(Shellard and Phillipson, 1964a, b)

+

-*M. rubrostipulata* (K.Schum.) Havil

(Hendrickson and Sims, 1963; Shellard and Lala, 1978)

-*Mitragyna speciosa* Korth

(Hendrickson and Sims, 1963; Shellard and Phillipson, 1964a; Beckett *et al.*,1965b; Shellard and Alam, 1968; Bindra, 1973)

-*M. stipulosa* (DC.) O.Kuntze

(Beckett *et al.*,1963a; Shellard and Alam, 1968; Shellard and Sarpong, 1970; Shellard, 1971; Houghton *et al.*,1976)

-*M. tubulosa* Havil.

(Rungsiyakul, 1973; Shellard and Rungsiyakul, 1973)

(+ = *anti*-rotundifoline N-oxide)

1.5.8 isorotundifoline (mitragynol, dihydrorotundifoline)

a) -*Uncaria attenuata* Korth : leaf

(Phillipson and Hemingway, 1975b; Phillipson *et al.*,1978)

-*U. bulusanensis* Elm. : leaf

(Phillipson and Hemingway, 1975b; Phillipson *et al.*,1978)

-*U. tomentosa* DC. : leaf, stem, flower

(Hemingway and Phillipson, 1974; Phillipson *et al.*,1978)

b) -*Mitragyna ciliata* Aubrev et Pellegr.

(Beckett *et al.*,1963b; Shellard and Alam, 1968; Shellard and Sarpong, 1970; Shellard, 1971)

-*M. inermis* (Willd.) O.Kuntze

(Shellard and Alam, 1968; Shellard and Sarpong, 1969, 1970; Shellard, 1971; Bindra, 1973)

-*M. parvifolia* (Roxb.) Korth

(Shellard and Phillipson, 1964b; Shellard *et al.*,1968b; Shellard and Alam, 1968; Shellard, 1971; Hemingway *et al.*, 1975)

-*Mitragyna rotundifolia* (Roxb.) O.Kuntze

(Beckett *et al.*,1963a; Shellard and Phillipson, 1964a, b)

-*M. rubrostipulata* (K. Schum.) Havil

(Shellard and Lala, 1978)

-*M. speciosa* Korth

(Shellard and Alam, 1968)

-*M. stipulosa* (DC.) O.Kuntze

(Beckett *et al.*,1963a; Shellard and Alam, 1968; Shellard, 1971; Houghton *et al.*,1976)

-*M. tubulosa* Havil

(Rungsiyakul, 1973; Shellard and Rungsiyakul, 1973)

1.5.9 speciofoline

a) -*Uncaria bulusanensis* Elm.

(Phillipson and Hemingway, 1975b; Phillipson *et al.*,1978)

b) -*Mitragyna speciosa* Korth

(Beckett *et al.*,1965b; Shellard and Alam, 1968; Shellard, 1971; Bindra, 1973; Hemingway *et al.*,1975; Shellard *et al.*,1978a)

1.6 Other Oxindole Alkaloids

1.6.1 dihydrocorynantheine pseudoindoxyl

a) -*Uncaria attenuata* Korth : leaf

(Phillipson and Hemingway, 1975b; Phillipson *et al.*,1978)

-*U. africana* (G. Don.) Baill. : leaf

(Phillipson *et al.*,1978)

1.6.2 yohimbine oxindole

a) -*Uncaria attenuata* Korth : leaf, stem bark, stem wood

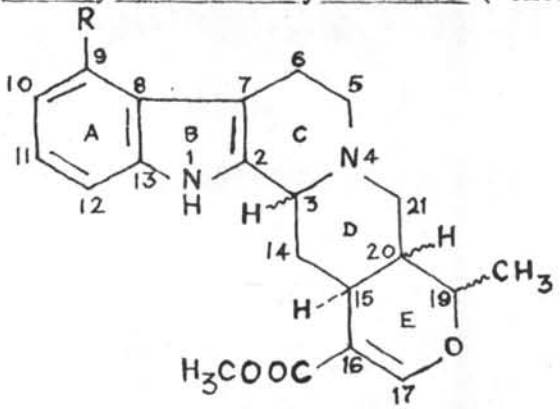
(Phillipson and Hemingway, 1975b; Phillipson *et al.*,1978)

= with its N-oxide

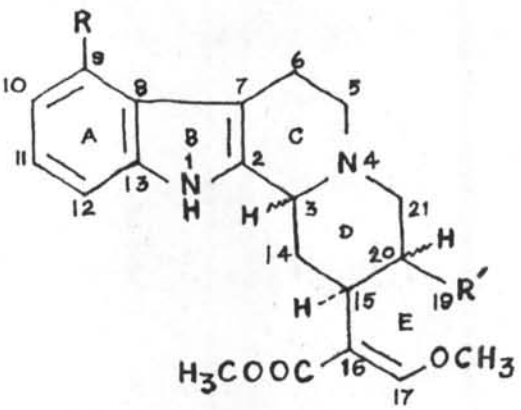
2. Basic structures of *Uncaria* alkaloids.

2.1 Heteroyohimbine alkaloids.

2.1.1 Pentacyclic heteroyohimbines (closed E ring)

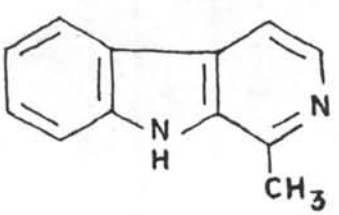


2.1.2 Tetracyclic heteroyohimbines (open E ring or E-*seco*)



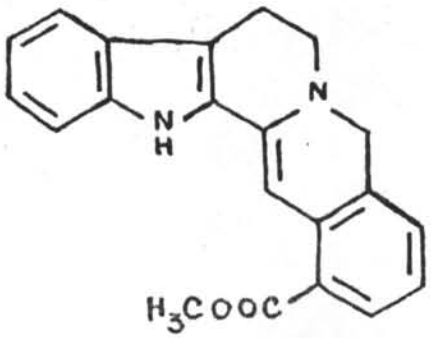
2.1.3 Other indole alkaloids.

2.1.3.1 β-carboline

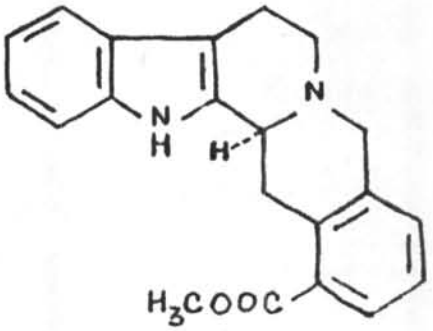


harmane

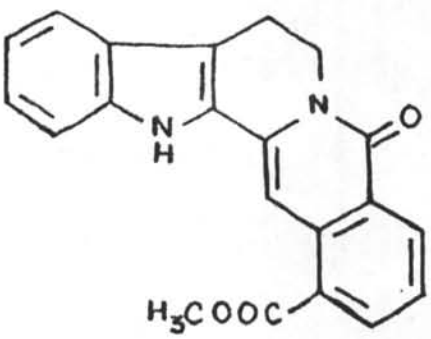
2.1.3.2 Gambirtannines.



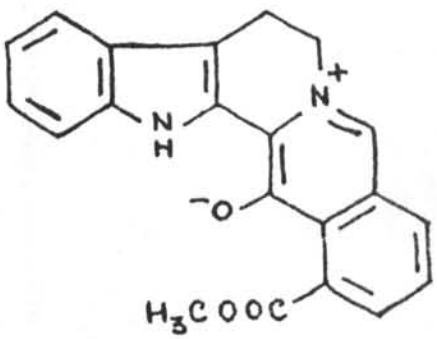
Gambirtannine



Dihydrogambirtannine

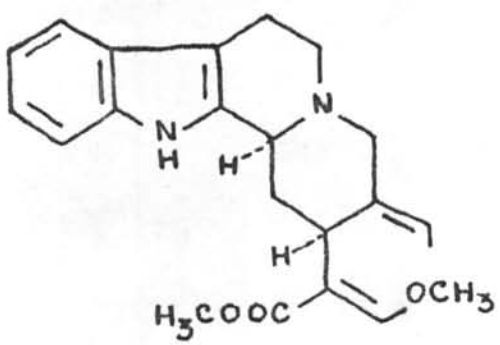


Oxygambirtannine

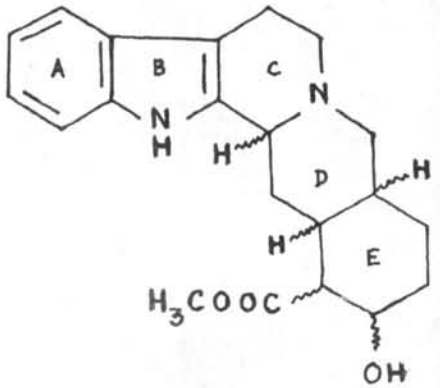


Neooxygambirtannine

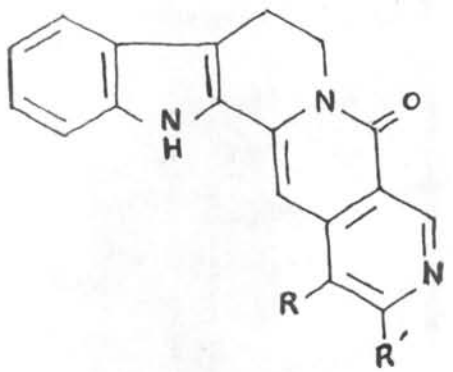
2.1.3.3 Geissoschizine methyl ether.



2.1.3.4 Yohimbine and its isomers.



2.1.3.5 Pyridino-indolo-quinolizidinones.

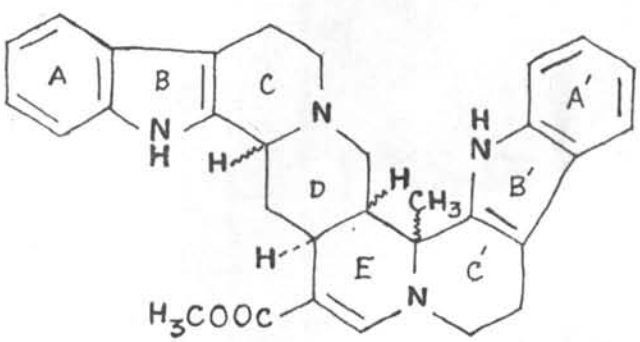


angustine, R = $-CH=CH_2$; R'= H

angustoline, R = $-CH(OH)CH_3$; R'= H

angustidine, R = H ; R'= $-CH_3$

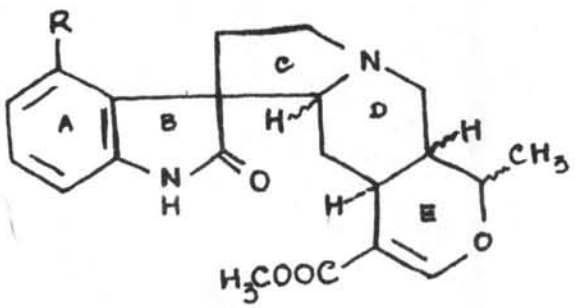
2.1.3.6 Roxburghines.



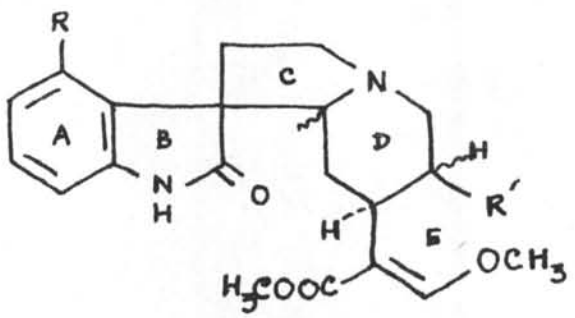
Roxburghines A, B, C, D, E

2.2 Oxindole alkaloids.

2.2.1 Pentacyclic oxindoles (closed E ring)

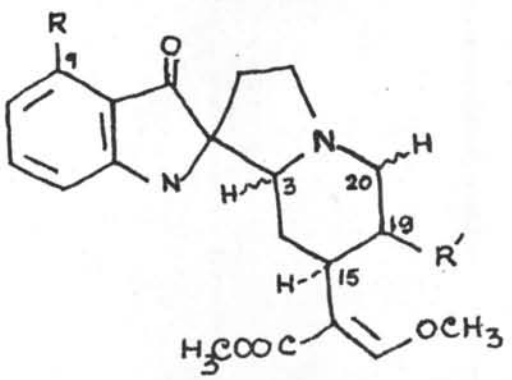


2.2.2 Tetracyclic oxindoles (open E ring or E-*seco*)

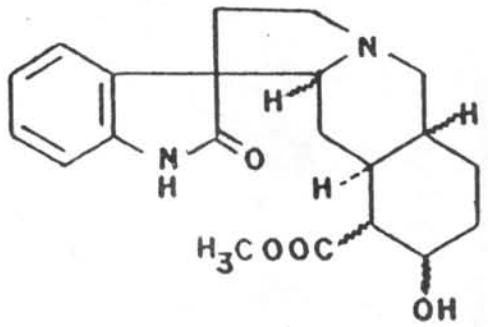


2.2.3 Other oxindole alkaloids.

2.2.3.1 Tetracyclic pseudoindoxyl



2.2.3.2 Yohimbine oxindole



3. Configurations of Heteroyohimbine and Oxindole Alkaloids.

The alkaloids have asymmetric centres at C(3), C(15), C(20) and all possess a C(15)-Hα configuration. For C(3) and C(20) there are 4 diastereoisomers possibly exist as follows:-

normal ; C(3)-Hα , C(20)-Hβ

pseudo ; C(3)-Hβ , C(20)-Hβ

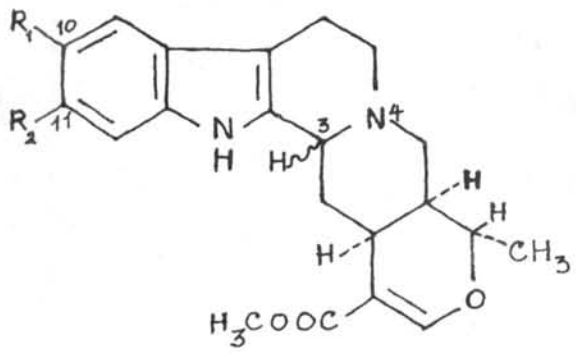
allo ; C(3)-Hα , C(20)-Hα

epiallo ; C(3)-Hβ , C(20)-Hα

The pentacyclic alkaloids have another asymmetric centre at C(19), i.e. $CH_3\alpha$ or β. The tetracyclic alkaloids may show geometric isomerisation because of the double bond between C(16) and C(17) but all known alkaloids possess a C(17)-H *cis* to the ester group on C(16).

Substitutions in the aromatic ring have been found at C(9) and C(14). The group at C(9) can be either hydroxy or methoxy group, while that at C(14) only hydroxy group is found. Recently, Ahond *et al* (1981) reported new indole alkaloids from trunk bark of *Ochrosia moorei*

F.Muell. ex Benth. with substituent groups at C(10) and C(11). Basic structures of the alkaloids are shown below :-



tetrahydroalstonine; $R_1=R_2=H$, C3-Hα

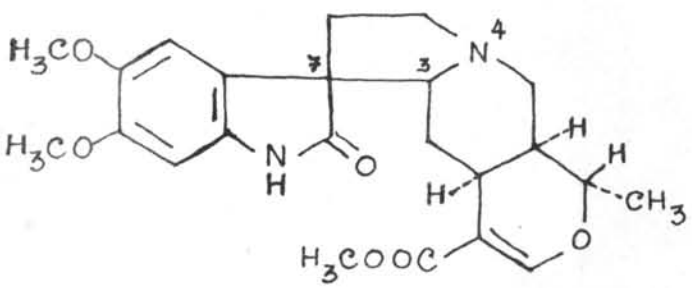
aricine; $R_1=OMe$, $R_2=H$, C3-Hα

reserpinine; $R_1=H$, $R_2=OMe$, C3-Hα

ochropposine; $R_1=R_2=OMe$, $\Delta^{3,4}$

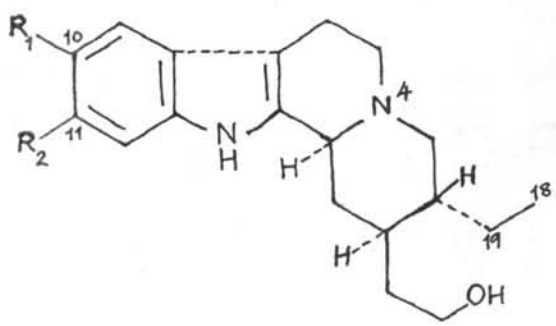
isoreserpiline; $R_1=R_2=OMe$, C3-Hα

reserpiline; $R_1=R_2=OMe$, C3-Hβ



rauvoxine; 7R,3R,4R

isocarapanaubine; 7S,3S,4R



10-hydroxy-dihydrocorynantheol;

$R_1=OH$, $R_2=H$

10-methoxy-3S,4R-dihydrocorynantheol N-oxide; $R_1=OMe$, $R_2=H$, $N_{4R}\rightarrow O$

3R,4S-reserpiline-N-oxide;

$R_1=OMe$, $R_2=H$, $N_{4S}\rightarrow O$

In the tetracyclic alkaloids the substituent group (R') may be either an ethyl or a vinyl group.

The oxindole alkaloids have an asymmetric centre at C(7) in two different ways. The A series are classified by the lactam carbonyl lying below the plane of the C/D ring and the B series by the lactam carbonyl lying above the plane of the C/D ring. Further, the lone pair electrons on N(4) of the oxindoles may either be on the same side of the C(7) as the lactam carbonyl group or on the opposite side and the alkaloids known respectively as *syn* and *anti* alkaloids (Finch and Taylor, 1962a,b; Shamma *et al.*,1967)

The oxindole alkaloids with *pseudo* configurations were believed to be too unstable to exist (Bindra,1973; Shellard *et al.*,1969b; Shellard and Houghton,1971). However, Brown and Platt (1976) had succeeded in synthesising the *pseudo* oxindole alkaloids from the condensation of dihydrosecologanin aglycone and 2-oxytryptamine. The synthesised alkaloids are reasonably stable.

Names and configurations of heteroyohimbine and oxindole alkaloids are summarised below.

a) Pentacyclic heteroyohimbines.

alkaloid	configuration	C(9)-R	C(19)-CH_3
ajmalicine	*normal*	H	α
3-isoajmalicine	*pseudo*	H	α
tetrahydroalstonine	*allo*	H	α
akuammigine	*epiallo*	H	α

alkaloid	configuration	C(9)-R	C(19)-CH_3
19-epiajmalicine	*normal*	H	β
19-epi-3-isoajmalicine	*pseudo*	H	β
rauniticine	*allo*	H	β
3-isorauniticine	*epiallo*	H	β
14-hydroxy-3-isorauni-ticine	*epiallo*	H and C(14)H=OH	β
isomitrajavine*	*normal*	OCH_3	α
(mitrajavine)	*pseudo*	OCH_3	α

Reference : Wenkert and Roychaudhuri, 1958;

Shamma and Richey, 1963;

Phillipson and Shellard, 1967;

Shellard and Sarpong, 1971b;

Saxton, 1973; Phillipson and Hemingway, 1975a;

Supavita, 1979; Ponglux *et al.*,1980.

b) Tetracyclic heteroyohimbines.

alkaloid	configuration	C(9)-R	C(20)-R'
dihydrocorynantheine	*normal*	H	CH_2-CH_3
hirsutine	*pseudo*	H	CH_2-CH_3
(corynantheidine)	*allo*	H	CH_2-CH_3
(isocorynantheidine)	*epiallo*	H	CH_2-CH_3
corynantheine	*normal*	H	$CH{=}CH_2$
hirsuteine	*pseudo*	H	$CH{=}CH_2$
epiallo-corynantheine	*epiallo*	H	$CH{=}CH_2$

alkaloid	configuration	C(9)-R	C(20)-R'
gambirine	*normal*	OH	CH_2-CH_3
(isogambirine)	*pseudo*	OH	CH_2-CH_3
(speciogynine)	*normal*	OCH_3	CH_2-CH_3
(mitraciliatine)	*pseudo*	OCH_3	CH_2-CH_3
(mitragynine)	*allo*	OCH_3	CH_2-CH_3
(speciociliatine)	*epiallo*	OCH_3	CH_2-CH_3
(paynantheine)	*normal*	OCH_3	CH=CH_2
(isopaynantheine)	*pseudo*	OCH_3	CH=CH_2

Reference : Beckett *et al.*,1966b; Phillipson and Shellard, 1966, 1967; Lee *et al.*,1967; Saxton, 1968; Trager *et al.*,1968b; Aimi *et al.*,1972; Phillipson and Hemingway, 1975a; Shellard *et al.*,1978b.

c) Other indole alkaloids.

Roxburghines

alkaloid	configuration	C(19)
Roxburghine B	*epiallo*	β
Roxburghine C	*normal*	α
Roxburghine D	*pseudo*	α
Roxburghine E	*pseudo*	β
Roxburghine X	not yet known	β

Reference : Phillipson *et al.*,1978; Herath *et al.*,1979.

d) Pentacyclic oxindoles.

alkaloid	configuration	C(7) series	C(9)-R	C(19)-CH_3
isomitraphylline	*normal*	A	H	α
mitraphylline	*normal*	B	H	α
isopteropodine (uncarine E)	*allo*	A	H	α
pteropodine (uncarine C)	*allo*	B	H	α
speciophylline (uncarine D)	*epiallo*	A	H	α
uncarine F	*epiallo*	B	H	α
uncarine A (isoformosanine)	*normal*	A	H	β
uncarine B (formosanine)	*normal*	B	H	β
(rauniticine oxindole A)	*allo*	A	H	β
(rauniticine oxindole B)	*allo*	B	H	β
(javaphylline)	*normal*	A	OCH_3	α
isojavaphylline	*normal*	B	OCH_3	α
gambirdine +	-	-	H	-
isogambirdine +	-	-	H	-

+Gambirdine and isogambirdine are two interconvertible stereoisomers of mitraphylline. There is no definitive information concerning their stereochemistry. (Saxton, 1973)

Reference : Beckett *et al.*,1966a; Shamma *et al.*,1967; Beecham *et al.*,1967a;

Shellard *et al.*, 1968a; Saxton, 1973; Phillipson and Hemingway, 1975a

e) Tetracyclic oxindoles.

alkaloid	configuration	C(7) series	C(9)-R	C(20)-R'
isorhynchophylline	*normal*	A	H	CH_2-CH_3
rhynchophylline	*normal*	B	H	CH_2-CH_3
corynoxine	*allo*	A	H	CH_2-CH_3
corynoxine B	*allo*	B	H	CH_2-CH_3
isocorynoxeine	*normal*	A	H	CH=CH_2
corynoxeine	*normal*	B	H	CH=CH_2
rotundifoline	*normal*	A	OH	CH_2-CH_3
isorotundifoline	*normal*	B	OH	CH_2-CH_3
(mitrafoline)	*allo*	A	OH	CH_2-CH_3
(isomitrafoline)	*allo*	B	OH	CH_2-CH_3
(isospeciofoline)	*epiallo*	A	OH	CH_2-CH_3
speciofoline	*epiallo*	B	OH	CH_2-CH_3
(rotundifoleine)	*normal*	A	OH	CH=CH_2
(isorotundifoleine)	*normal*	B	OH	CH=CH_2
(rhynchociline)	*normal*	A	OCH_3	CH_2-CH_3
(ciliaphylline)	*normal*	B	OCH_3	CH_2-CH_3
(mitragynine oxindole A)	*allo*	A	OCH_3	CH_2-CH_3
(mitragynine oxindole B)	*allo*	B	OCH_3	CH_2-CH_3

alkaloid	configuration	C(7) series	C(9)-R	C(20)-R'
(isospecionoxeine)	*normal*	A	OCH_3	$CH=CH_2$
(specionoxeine)	*normal*	B	OCH_3	$CH=CH_2$

Reference : Trager *et al.*,1968a ; Phillipson and Shellard, 1968 ; Saxton, 1973 ; Phillipson and Hemingway, 1975a ; Hemingway *et al.*, 1975

f) Other oxindole alkaloid

tetracyclic pseudoindoxyl :-

dihydrocorynantheine pseudoindoxyl

C(9)-R = H , C(19) R' = CH_2-CH_3 , C(3)H α , C(20)H β, C(19)H β

Reference : Phillipson and Hemingway, 1975b ; Phillipson *et al.*,1978.

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* = semi-synthetic

(_) = not yet isolated from *Uncaria* species.

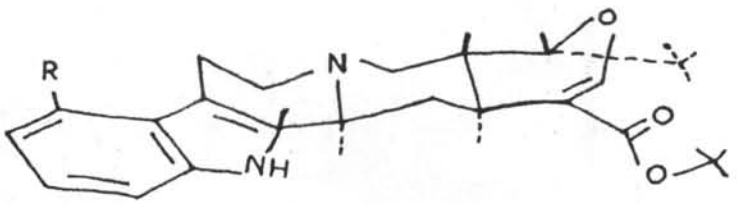
4. Preferred conformations of heteroyohimbine and oxindole alkaloids

4.1 Heteroyohimbine alkaloids

The preferred conformations of heteroyohimbine alkaloids were established as follows (Trager *et al.*,1967; Hart *et al.*,1967; Beecham *et al.*,1967a; Phillipson and Shellard,1967) :-

4.1.1 Pentacyclic heteroyohimbines

Normal

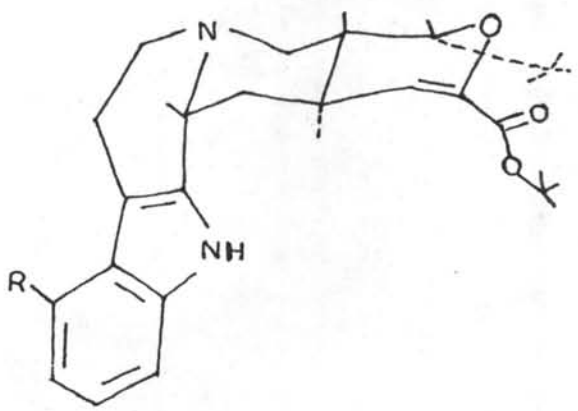


R = H : ajmalicine

R = H and C(19)$CH_3\beta$: 19-epiajmalicine

R = OCH_3 : isomitrajavine*

Pseudo

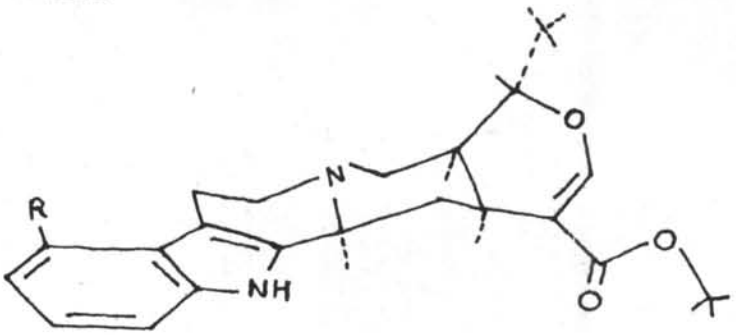


R = H : 3-isoajmalicine

R = H and C(19)$CH_3\beta$: 19-epi-3-isoajmalicine

R = OCH_3 : (mitrajavine)

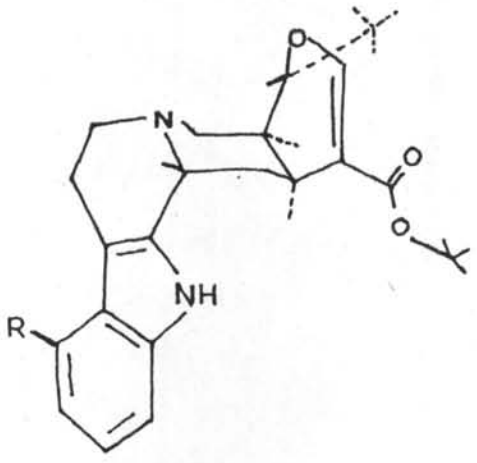
Allo



R = H : tetrahydroalstonine

R = H and C(19)-$CH_3\beta$: **rauniticine**

Epiallo



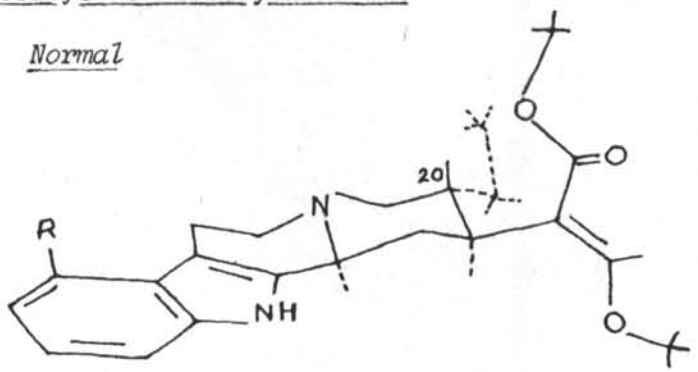
R = H : akuammigine

R = H and C(19)-$CH_3\beta$: (3-isorauniticine)

R = H, C(14)H = OHβ and C(19)-$CH_3\beta$: 14-hydroxy-3-isorauniticine

4.1.2 Tetracyclic heteroyohimbines

Normal



R = H : dihydrocorynantheine

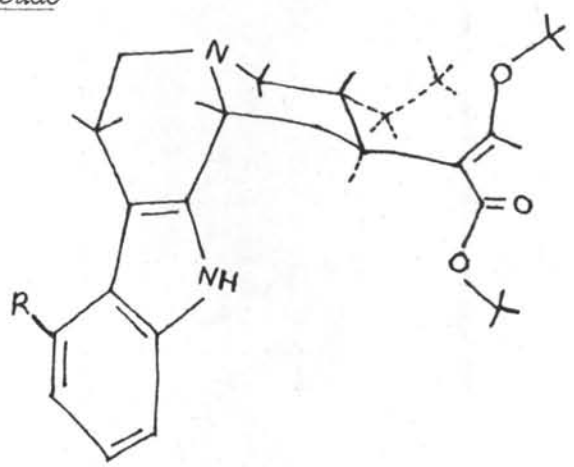
R = H and C(20)Et = vinyl : corynantheine

R = OH : gambirine

R = OCH_3 : (speciogynine)

R = OCH_3 and C(20)Et = vinyl : (paynantheine)

Pseudo



R = H : hirsutine

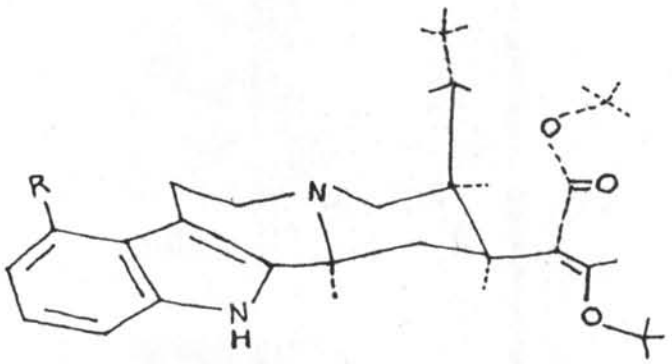
R = H and C(20)Et = vinyl : hirsuteine

R = OH : (isogambirine)

R = OCH_3 : (mitraciliatine)

R = OCH_3 and C(20)Et = vinyl : (isopaynantheine)

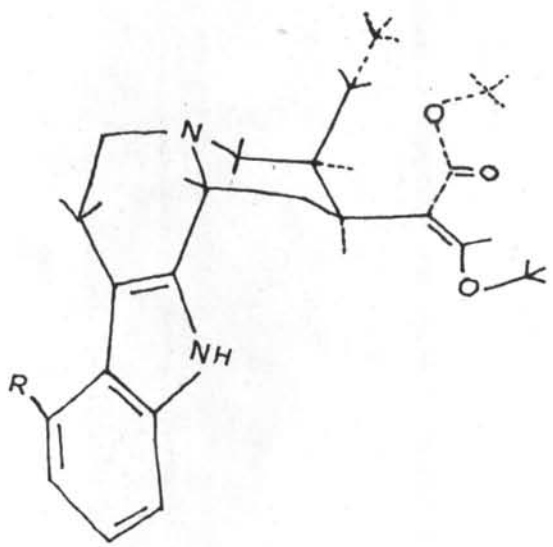
Allo



R = H : (corynantheidine)

R = OCH_3 : (mitragynine)

Epiallo



R = H : (isocorynantheidine)

R = H and C(20)Et = vinyl : *epiallo*-corynantheine

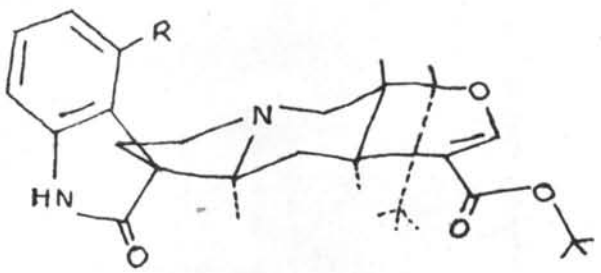
R = OCH_3 : (speciociliatine)

4.2 Oxindole alkaloids

The preferred conformations of oxindole alkaloids were established as follows. (Phillipson and Shellard, 1966; Trager *et al.*, 1967b; Chan, 1969; Bindra, 1973; Saxton, 1973) :-

4.2.1 Pentacyclic oxindoles

Normal A

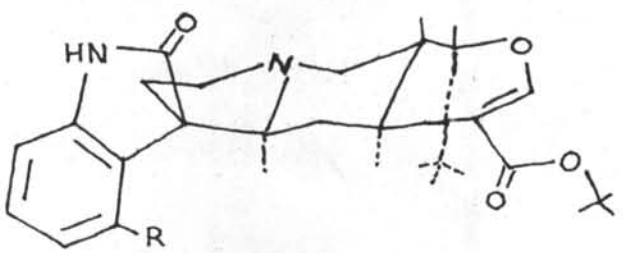


R = H : isomitraphylline

R = H and C(19)-$CH_3\beta$: uncarine A (isoformosanine)

R = OCH_3 : (javaphylline)

Normal B

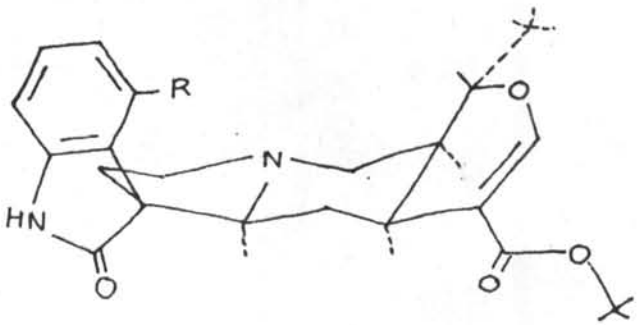


R = H : mitraphylline

R = H and C(19)-$CH_3\beta$: uncarine B (formosanine)

R = OCH_3 : isojavaphylline*

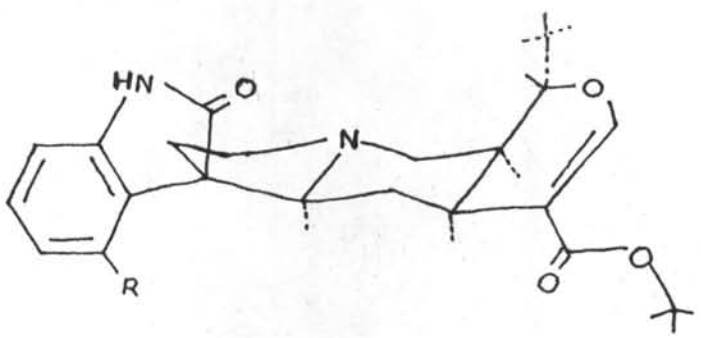
Allo A



R = H : isopteropodine (uncarine E)

R = H and C(19)-$CH_3\beta$: (rauniticine oxindole A)

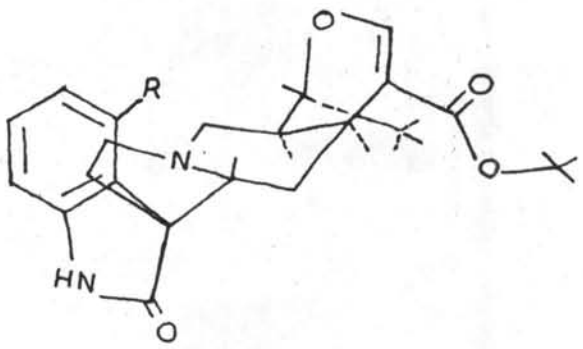
Allo B



R = H : pteropodine (uncarine C)

R = H and C(19)-$CH_3\beta$: (rauniticine oxindole B)

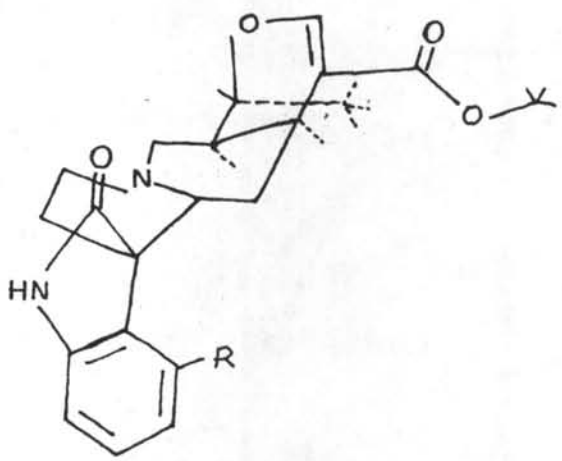
Epiallo A



R = H : speciophylline (uncarine D)

R = H and C(19)-$CH_3\beta$: (rauniticine *epi*-oxindole A)

Epiallo B

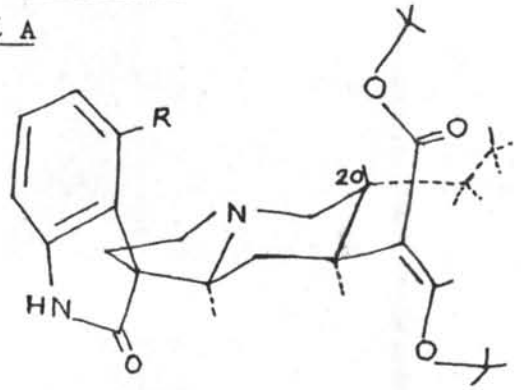


R = H : uncarine F

R = H and C(19)-$CH_3\beta$: (rauniticine *epi*-oxindole B)

4.2.2 Tetracyclic oxindoles

Normal A



R=H : isorhynchophylline

R=H and C(20)Et = vinyl : isocorynoxeine

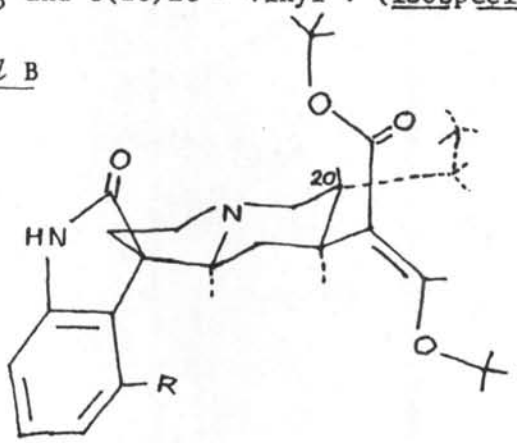
R=OH : rotundifoline

R=OH and C(20)Et = vinyl : (rotundifoleine)

R=OCH_3 : (rhynchociline)

R=OCH_3 and C(20)Et = vinyl : (isospecionoxeine)

Normal B



R=H : rhynchophylline

R=H and C(20)Et = vinyl : corynoxeine

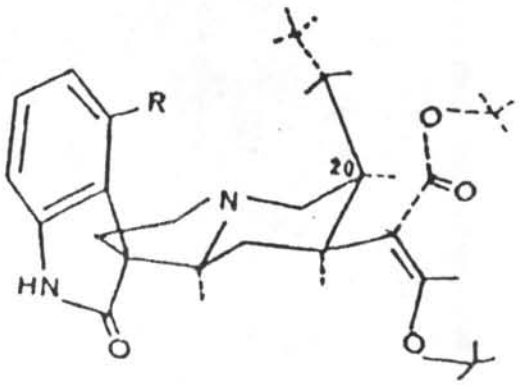
R=OH : isorotundifoline

R=OH and C(20)Et = vinyl : (isorotundifoleine)

R=OCH_3 : (ciliaphylline)

R=OCH_3 and C(20)Et = vinyl : (specionoxeine)

Allo A

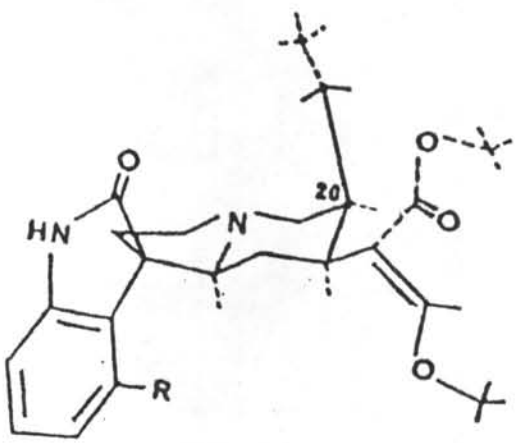


R = H:corynoxine

R = OH:(mitrafoline)

R = OCH_3:(mitragynine oxindole A)

Allo B

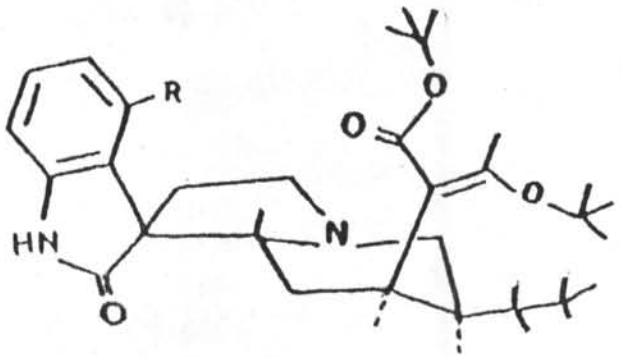


R = H:corynoxine B

R = OH;(isomitrafoline)

R = OCH_3:(mitragynine oxindole B)

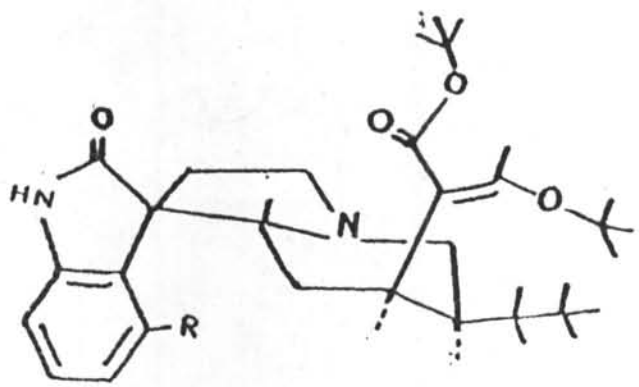
Epiallo A



R = OH: (isospeciofoline)

R = OCH_3: speciociliatine oxindole A*

Epiallo B



R = OH: speciofoline

R = OCH_3: speciociliatine oxindole B*

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* = semi-synthetic

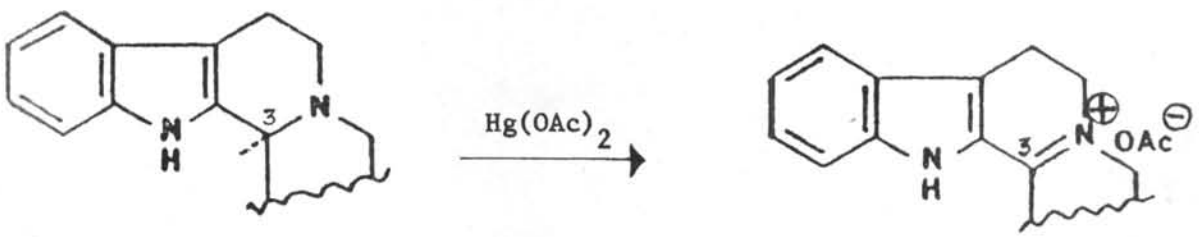
(_) = not yet isolated from *Uncaria* species

5. Chemical Transformation

5.1 Isomerisation

5.1.1 Isomerisation of heteroyohimbine alkaloids

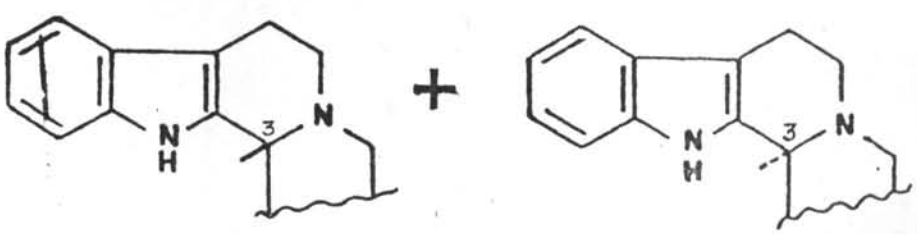
The isomerisation of heteroyohimbine alkaloids may be obtained at C(3) by many procedures. Yohimbine, the *normal* heteroyohimbine alkaloid, was isomerised by mercuric acetate to 3-dehydroyohimbine and was reduced by zinc and acetic acid or hydrochloric acid to pseudoyohimbine, the *pseudo* hetero - yohimbine. The isomerisation from C(3)-Hα to C(3)-Hβ isomer are shown below:-



(C3-Hα heteroyohimbine:- *normal, allo*)

(3-dehydro compound)

Zn/HOAc or HCl



(C3-Hβ heteroyohimbine:- *pseudo, epiallo*)

(C3-Hα heteroyohimbine:- *normal, allo*)

(Weisenborn and Diassi,1956; Wenkert and Roychaudhuri,1956,1958)

Experiments have shown that compounds with the *normal* and *allo* configurations are more readily oxidised at C(3) by mercuric acetate than those with the *pseudo* and *epiallo* configurations (Leonard and Morrow, 1958).

The conversion of heteroyohimbine alkaloids into their corresponding isomers are summarised in the following table :-

Conversion	Reference
ajmalicine (*normal*) ⟶ 3-isoajmalicine (*pseudo*)	Wenkert and Roychaudhuri, 1956; Wenkert,1961.
tetrahydroalstonine (*allo*) ⟶ akuammigine (*epiallo*)	Wenkert and Roychaudhuri, 1956; Wenkert,1961.
19-*epi*-ajmalicine (*normal*) ⟶ 19-*epi*-3-isoajmalicine (*pseudo*)	Phillipson and Hemingway, 1975b.
rauniticine (*allo*) ⟶ 3-isorauniticine (*epiallo*)	Shamma and Richey,1963.
mitrajavine (*pseudo*) ⟶ isomitrajavine (*normal*)	Shellard and Sarpong,1971b.
dihydrocorynantheine (*normal*) ⇌ hirsutine (*pseudo*)	Trager *et al.*,1968b.
corynantheidine (*allo*) ⟶ isocorynantheidine (*epiallo*)	Beckett *et al.*,1969; Shellard *et al.*,1978a.
speciogynine (*normal*) ⟶ mitraciliatine (*pseudo*)	Trager *et al.*,1968b.
mitragynine (*allo*) ⟶ speciociliatine (*epiallo*)	Trager *et al.*,1968b; Shellard *et al.*,1978a.
paynantheine (*normal*) ⟶ isopaynantheine (*pseudo*)	Beckett *et al.*,1969; Shellard *et al.*,1978a.

5.1.2 Isomerisation of oxindole alkaloids

The conversion of oxindole alkaloids into their stereoisomers under equilibrium conditions at the C(3) and/or C(7) centres by treating with acetic acid or pyridine gives a mixture of two stereoisomers, the oxindoles A and B. The stronger base, B isomers, predominate after acid treatment while the weaker base, A isomers, predominate after refluxing in pyridine (Finch and Taylor, 1962b).

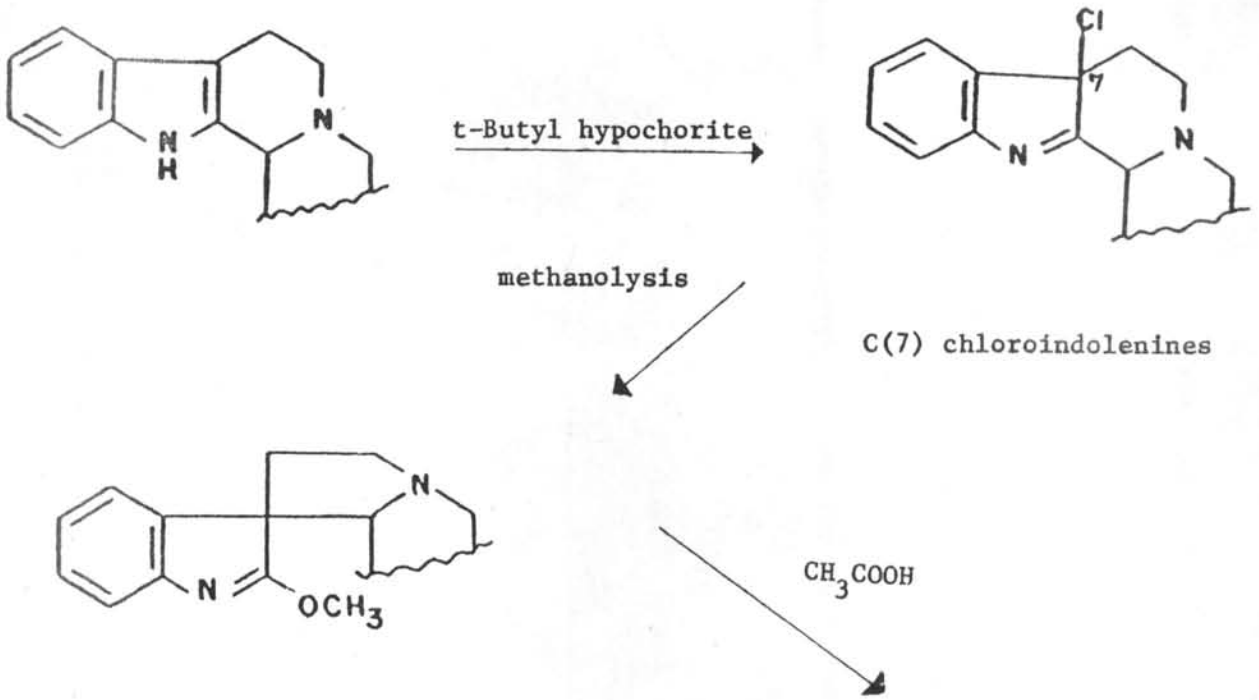
Some isomerisation of oxindole alkaloids are summarised in the following table :-

starting isomer	reagent	isomerisation product	reference
Isomitraphylline or Mitraphylline	pyridine	80% Isomitraphylline(A), 20% Mitraphylline(B)	Seaton *et al.*, 1960
	acetic acid	20% Isomitraphylline(A), 80% Mitraphylline(B)	Beckett *et al.*, 1966a
Isopteropodine	pyridine	100% Isopteropodine(A)	Beecham *et al.*, 1968
Pteropodine	pyridine	10% Isopteropodine(A), 90% Pteropodine(B)	Beecham *et al.*, 1968
Speciophylline	pyridine	20% Isopteropodine(A), 30% Speciophylline(A), 20% Pteropodine(B), 30% Uncarine F (B)	Beecham *et al.*, 1968
Uncarine F	pyridine	20% Isopteropodine(A), 10-20% Speciophylline(A), 20% Pteropodine(B), 40-50% Uncarine F (B)	Beecham *et al.*, 1968
Pteropodine or Isopteropodine or Speciophylline or Uncarine F	acetic acid	10% Isopteropodine(A), 40% Speciophylline(A), 40% Pteropodine(B), 10% Uncarine F (B)	Beecham *et al.*, 1968
Uncarine A or Uncarine B	pyridine	80% Uncarine A (A), 20% Uncarine B (B)	Seaton *et al.*, 1960

starting isomer	reagent	isomerisation product	reference
Isorhynchophylline or Rhynchophylline	pyridine	70%Isorhynchophylline(A), 30%Rhynchophylline(B)	Seaton *et al.*, 1960
	pyridine	80%Isorhynchophylline(A), 20%Rhynchophylline(B)	Trager *et al.*, 1968a
	acetic acid	20%Isorhynchophylline(A), 80%Rhynchophylline(B)	Trager *et al.*, 1968a
Corynoxine or Corynoxine B	pyridine	80%Corynoxine(A), 20%Corynoxine B (B)	Trager *et al.*, 1968a
	acetic acid	20%Corynoxine(A), 80%Corynoxine B (B)	Trager *et al.*, 1968a
Rotundifoline or Isorotundifoline	pyridine	90%Rotundifoline(A), 10%Isorotundifoline(B)	Trager *et al.*, 1968a
	acetic acid	60%Rotundifoline(A), 40%Isorotundifoline(B)	Trager *et al.*, 1968a
Mitrafoline or Speciofoline	pyridine	40%Mitrafoline(A), 10%Isospeciofoline(A), 10%Isomitrafoline(B), 40%Speciofoline(B)	Hemingway *et al.*, 1975
	acetic acid	50%Mitrafoline(A), 10%Isospeciofoline(A), 15%Isomitrafoline(B), 25%Speciofoline(B)	Hemingway *et al.*, 1975
Isomitrafoline or Isospeciofoline	pyridine	major products:- Mitrafoline&Speciofoline minor products:- Isomitrafoline and Isospeciofoline	Hemingway *et al.*, 1975
Rhynchociline or Ciliaphylline	pyridine	35%Rhynchociline(A), 65%Ciliaphylline(B)	Trager *et al.*, 1968a
	acetic acid	50%Rhynchociline(A), 50%Ciliaphylline(B)	Trager *et al.*, 1968a
Specionoxeine or Isospecionoxeine	pyridine	65%Specionoxeine(A), 35%Isospecionoxeine(B)	Trager *et al.*, 1968a
	acetic acid	50%Specionoxeine(A), 50%Isospecionoxeine(B)	Trager *et al.*, 1968a

5.2 Conversion of heteroyohimbine to oxindole alkaloids.

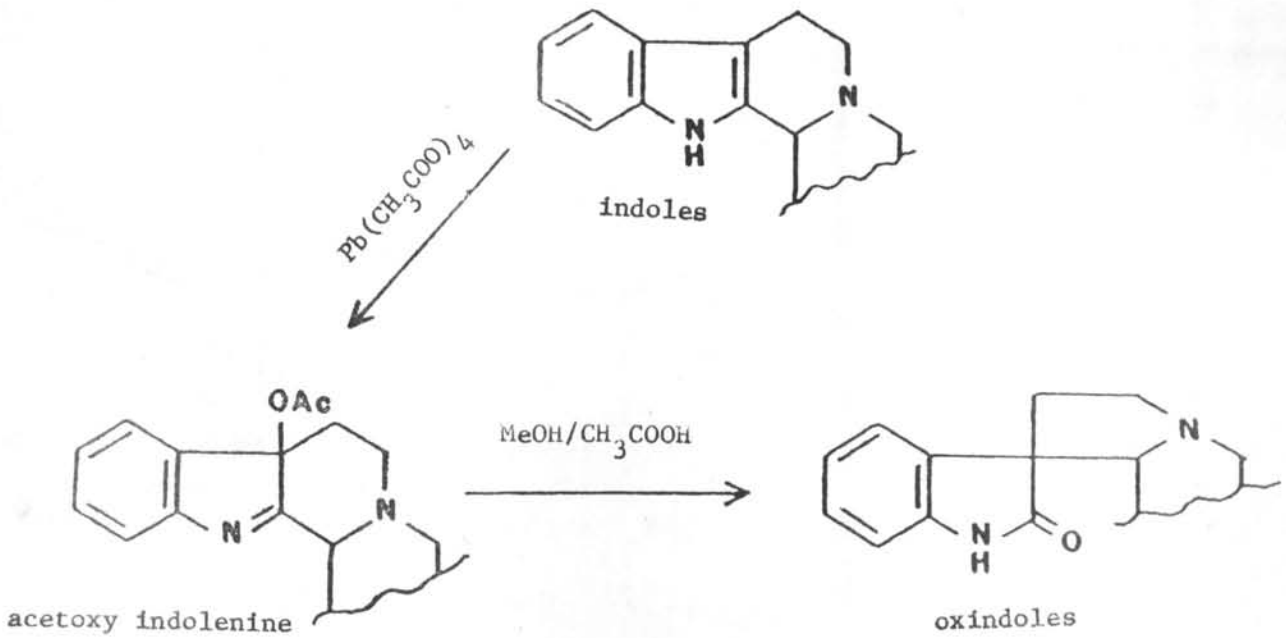
Yohimbine and heteroyohimbine alkaloids were reported by Finch and Taylor (1962a,b) and Shavel and Zinnes (1962) to be transformed into a mixture of epimeric C(7) chloroindolenines by the action of tertiary-butyl hypochlorite. Methanolysis gave the imido ether which on hydrolysis in aqueous acetic acid yeild the stronger base, oxindole B and the weaker one, oxindole A.



The conversion of some heteroyohimbine alkaloids to their corresponding oxindoles were performed as follows:-

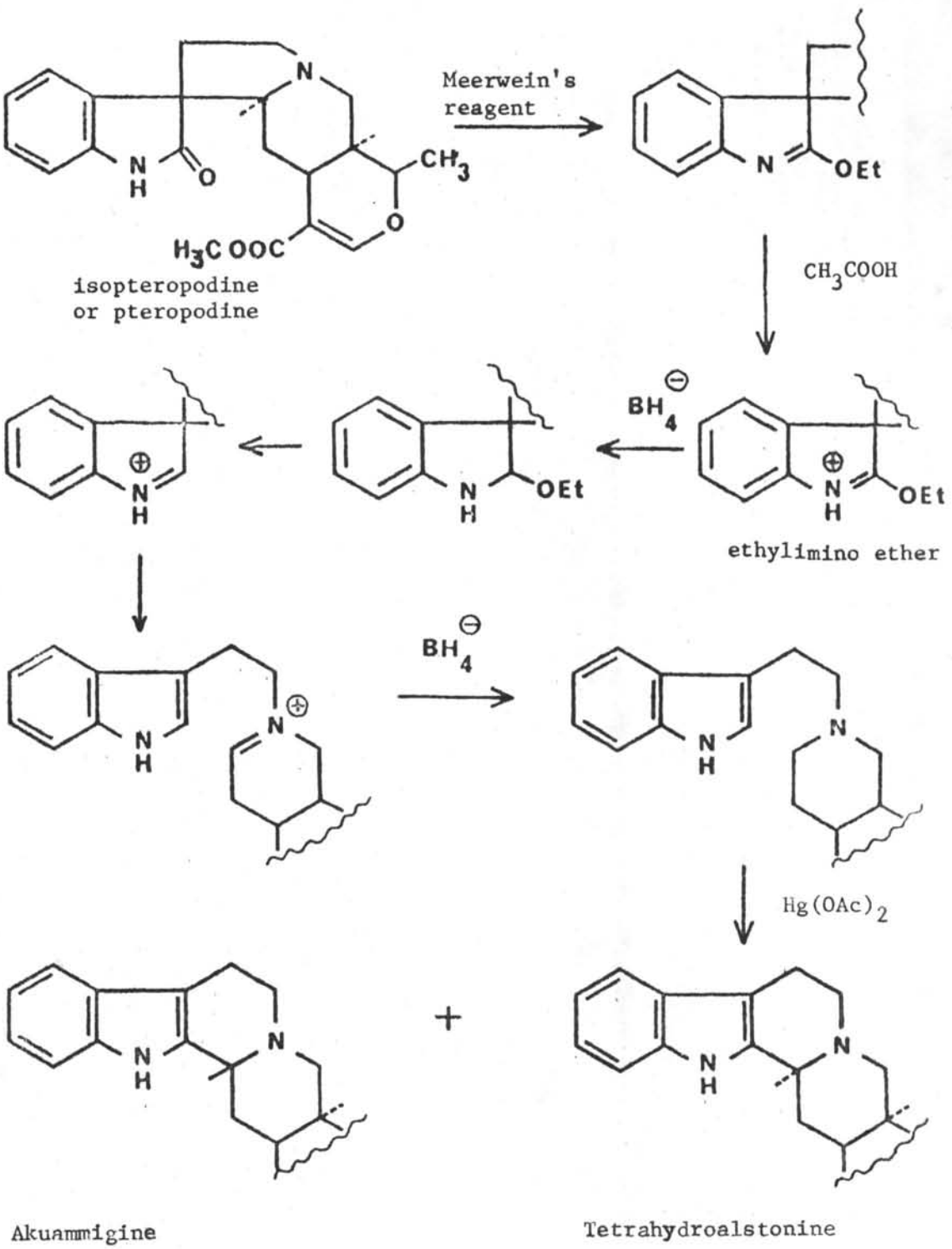
Heteroyohimbine	Oxindole	Reference
ajmalicine *(normal)*	isomitraphylline *(normal* A)	Shavel and Zinnes,1962;
	mitraphylline *(normal* B)	Finch and Taylor,1962a.
tetrahydroalstonine *(allo)*	isopteropodine *(allo* A)	Hart *et al*,1967.
	pteropodine *(allo* B)	
	speciophylline *(epiallo* A)	
	uncarine F *(epiallo* B)	
mitrajavine *(pseudo)*	javaphylline *(normal* A)	Shellard and Sarpong,1971a
	isojavaphylline *(normal* B)	
corynantheine *(normal)*	corynoxeine *(normal* B)	Finch and Taylor,1962b.
corynantheidine *(allo)*	corynoxine *(allo* A)	Trager *et al.*,1968a;
	corynoxine B *(allo* B)	Beckett *et al.*,1969.
dihydrocorynantheine *(normal)*	isorhynchophylline *(normal* A)	Finch and Taylor,1962a; Trager *et al.*,1968a.
	rhynchophylline *(normal* B)	
mitragynine *(allo)*	mitragynine oxindole A and B *(allo* A and B)	Beckett *et al.*,1969.

Using lead tetra-acetate the heteroyohimbines could be converted to oxindoles via acetoxy indolenine, which on refluxing with methanol containing acetic acid gives the oxindoles (Hart *et al.*,1967). This method were used to prepare isopteropodine, pteropodine, speciophylline and uncarine F from the heteroyohimbine, tetrahydroalstonine.



5.3 Conversion of oxindole to heteroyohimbine alkaloids

Aimi *et al.*(1972) transformed oxindoles into heteroyohimbines by using Meerwein's reagent in acetic acid to give ethylimino ethers. There were oxidised by mercuric acetate to yeild heteroyohimbines. Pteropodine and isopteropodine were transformed by this method and each yielded the corresponding heteroyohimbines, tetrahydroalstonine and akuammigine. Isorhynchophylline were also converted into hirsutine and dihydrocorynantheine. The transformation of pteropodine is described below:-


Meerwein's reagent
isopteropodine or pteropodine
CH_3COOH
ethylimino ether
$BH_4^\ominus$
$BH_4^\ominus$
$Hg(OAc)_2$
Akuammigine
Tetrahydroalstonine

5.4 The interconversion of pentacyclic and tetracyclic oxindole alkaloids.

Houghton and Shellard(1973) proposed that the pentacyclic oxindoles might arised by the ring closure of the tetracyclic oxindoles. The presence of the C(20)vinyl tetracyclic oxindoles, isocorynoxeine and corynoxeine, in *Mitragyna* plants containing mitraphylline and rhynchophylline suggested that they might be involved as intermediates.

In vivo ^{14}C-rhynchophylline, the tetracyclic oxindole, was fed below the leaf base of young plants of *Mitragyna parvifolia* (Roxb.) Korth. and mitraphylline, the pentacyclic oxindole was detected(Houghton and Shellard,1973). The tetracyclic oxindoles are present in the xylem, but the pentacyclic oxindoles are present in the leaves. E-ring closure occurs in the xylem of the leaf base 24 hours after the plant had been fed with active rhynchophylline, radioactive corynoxeine and mitraphylline were also detected in the leaf.

When ^{14}C-mitraphylline was fed into the stem bark, radioactivity was detected in the corynoxeine and rhynchophylline lower down the stem indicating that the reverse process, the conversion of pentacyclic to tetracyclic took place, with corynoxeine as an intermediate (Houghton and Shellard,1973,1974).

6. Alkaloid N-oxides

Shellard and Phillipson in 1964(a) reported the presence of alkaloids in the leaves of *Mitragyna rotundifolia* (Roxb.) O.Kuntze which remained on the base line of thin layer chromatograms with various solvent system, as sometimes they were called the "base-line" alkaloids. Merlini, Nasini and Phillipson (1972 b) believed these alkaloids not to be artifacts.

There were two methods used in preparing alkaloid N-oxides. The first method was to treat the base alkaloid with hydrogen peroxide overnight, heat on water bath for 30 minutes and further with platinum wire for 5 minutes (Shellard *et al.*,1971; Phillipson *et al* .,1973a). The second method was to oxidise the base alkaloid with *m*-chloroperbenzoic acid in chloroform (Phillipson *et al.*,1973 a).

For tetracyclic oxindole N-oxides, it has been shown that the B series oxindoles give only one N-oxide, where as those in A series give two form of N-oxides, an *anti* and a *syn* configurations.

6.1 Alkaloid N-oxides isolated from *Uncaria* and *Mitragyna* species

The N-oxides of many alkaloids have been reported to be present naturally and characterised from species of *Mitragyna* and *Uncaria* as summarised in the following table.

Alkaloid N-oxides	Botanical source	Reference
4(R)-Akuammigine N-oxide 4(S)-Akuammigine N-oxide	*Uncaria* sp., *Mitragyna parvifolia*	Merlini *et al.*,1972b; Shellard and Houghton, 1976.

Alkaloid N-oxides	Botanical source	Reference
4(R)-Tetrahydroalstonine N-oxide	*Uncaria* sp.	Merlini *et al.*, 1972b.
Dihydrocorynantheine N-oxide	*U. tomentosa*	Hemingway and Phillipson, 1974.
Hirsutine N-oxide	*U. tomentosa*	Hemingway and Phillipson, 1974.
Isomitraphylline N-oxide	*U. longiflora*	Phillipson and Hemingway, 1973b.
Mitraphylline N-oxide	*U. longiflora*	Phillipson and Hemingway, 1973b.
Isopteropodine N-oxide	*U. bernaysii*	Phillipson and Hemingway, 1973a.
Pteropodine N-oxide	*U. longiflora*	Phillipson and Hemingway, 1973b.
Speciophylline N-oxide	*U. bernaysii*, *U. longiflora*, *M. parvifolia*	Phillipson and Hemingway, 1973a,b; Shellard and Houghton, 1974.
Uncarine F N-oxide	*M. parvifolia*	Shellard and Houghton, 1974.
Anti-Isorhynchophylline N-oxide	*M. inermis*	Shellard *et al.*, 1971; Phillipson *et al.*, 1973a.
Syn-Isorhynchophylline N-oxide	*M. inermis*	Shellard *et al.*, 1971; Phillipson *et al.*, 1973a.
Rhynchophylline N-oxide	*M. inermis*	Shellard *et al.*, 1971; Phillipson *et al.*, 1973a.
Anti-Rotundifoline N-oxide	*M. rubrostipulata*	Shellard *et al.*, 1977.

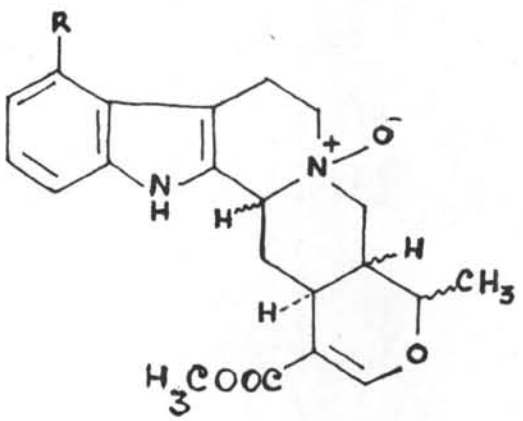
Alkaloid N-oxides	Botanical source	Reference
Syn-Rotundifoline N-oxide	*M. rubrostipulata*	Shellard *et al.*,1977.
Isorotundifoline N-oxide	*M. rubrostipulata*	Shellard *et al.*,1977.
Ciliaphylline N-oxide	*M. tubulosa*	Phillipson *et al.*, 1973a.

(Phillipson and Handa, 1978)

6.2 Basic structure and configuration of alkaloid N-oxides

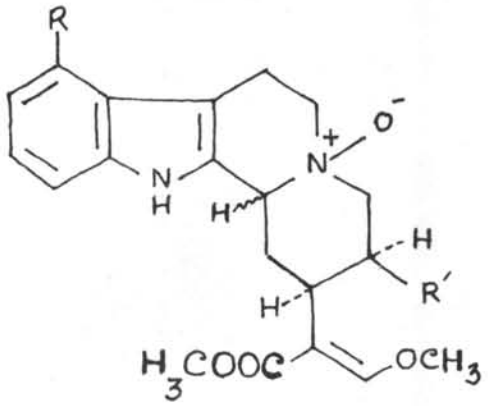
6.2.1 Heteroyohimbine N-oxides

6.2.1.1 Pentacyclic heteroyohimbine N-oxides



Alkaloid	Configuration	Reference
(4R)-Tetrahydroalstonine N-oxide	*allo*	Merlini *et al.*,1972b.
(4R)-Akuammigine N-oxide	*epiallo*	Merlini *et al.*,1972b.
(4S)-Akuammigine N-oxide	*epiallo*	Merlini *et al.*,1972b.

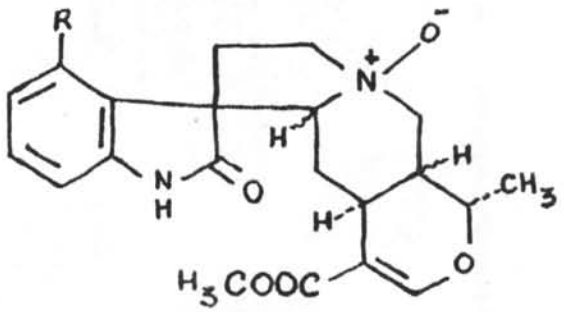
6.2.1.2 Tetracyclic heteroyohimbine N-oxides



Alkaloid	Configuration	Reference
Dihydrocorynantheine N-oxide	*normal*	Hemingway and Phillipson, 1974.
Hirsutine N-oxide	*pseudo*	Hemingway and Phillipson, 1974.

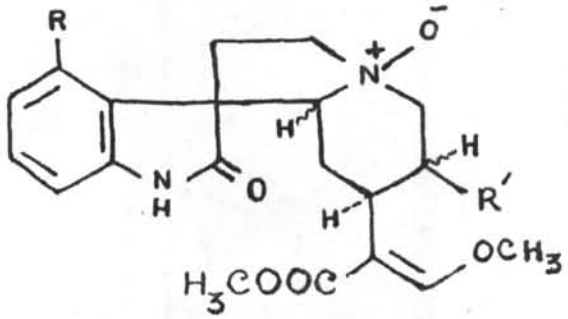
6.2.2 Oxindole N-oxides

6.2.2.1 Pentacyclic oxindole N-oxides



Alkaloid	Configuration	Reference
Isomitraphylline N-oxide	*normal* A	Phillipson and Hemingway, 1973a, b; Shellard and Houghton, 1974; Phillipson *et al.*, 1978.
Mitraphylline N-oxide	*normal* B	Phillipson and Hemingway, 1973a, b; Shellard and Houghton, 1974; Phillipson *et al.*, 1978
Isopteropodine N-oxide	*allo* A	Phillipson *et al.*, 1978
Pteropodine N-oxide	*allo* B	Phillipson *et al.*, 1978
Speciophylline N-oxide	*epiallo* A	Shellard and Houghton, 1974; Phillipson *et al.*, 1978
Uncarine F N-oxide	*epiallo* B	Shellard and Houghton, 1974; Phillipson *et al.*, 1978

6.2.2.2 Tetracyclic Oxindole N-oxides



Alkaloid	Configuration	Reference
Isorhynchophylline N-oxide	*normal* A *syn-* and *anti-*	Phillipson *et al.*,1978; Phillipson *et al.*,1973a; Shellard *et al.*,1971.
Rhynchophylline N-oxide	*normal* B	Phillipson *et al.*,1973a; Shellard and Lala,1978; Shellard *et al.*,1971.
Rotundifoline N-oxide	*normal* A *syn-* and *anti-*	Shellard *et al.*,1977; Shellard and Lala,1978.
Isorotundifoline N-oxide	*normal* B	Shellard *et al.*,1977; Shellard and Lala,1978.
Rhynchociline N-oxide*	*normal* A *syn-* and *anti-*	Phillipson *et al.*,1973a.
Ciliaphylline N-oxide	*normal* B	Phillipson *et al.*,1973a; Rungsiyakul,1973; Shellard and Rungsiyakul, 1973.

* = semi-synthetic

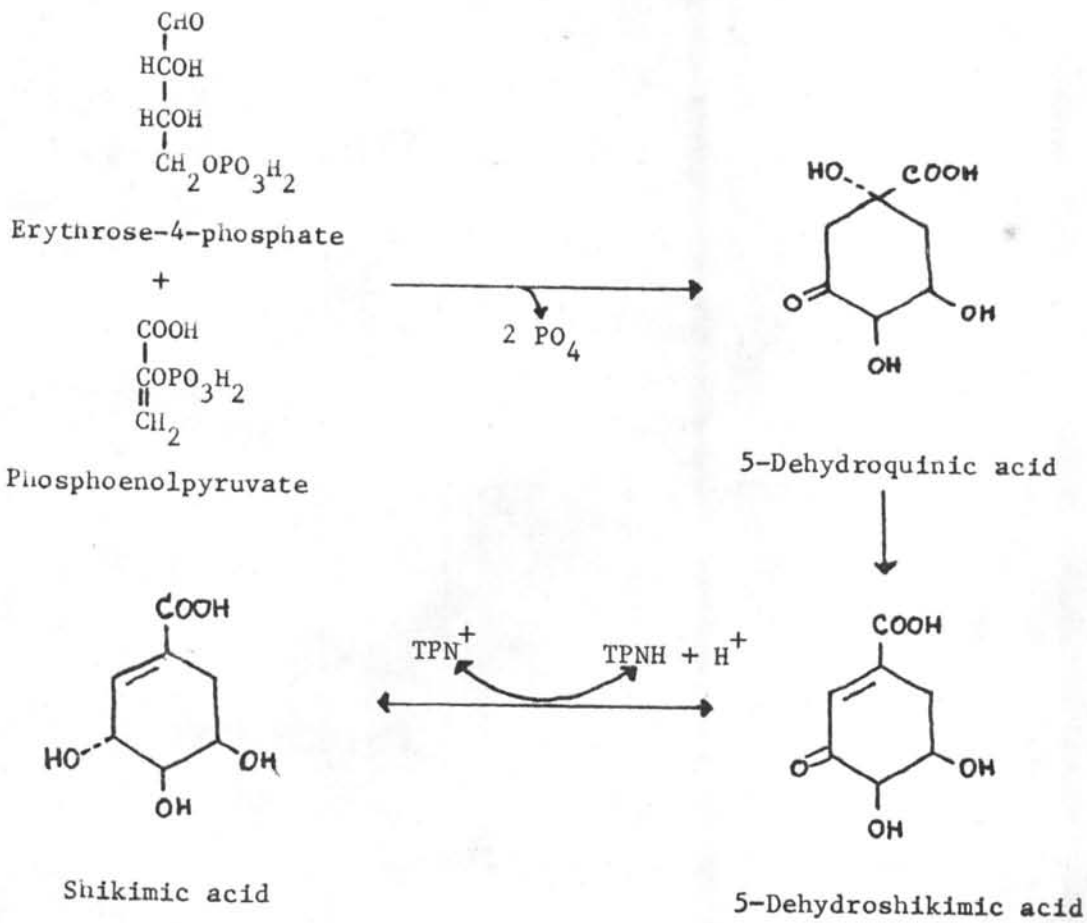
7. Biogenesis

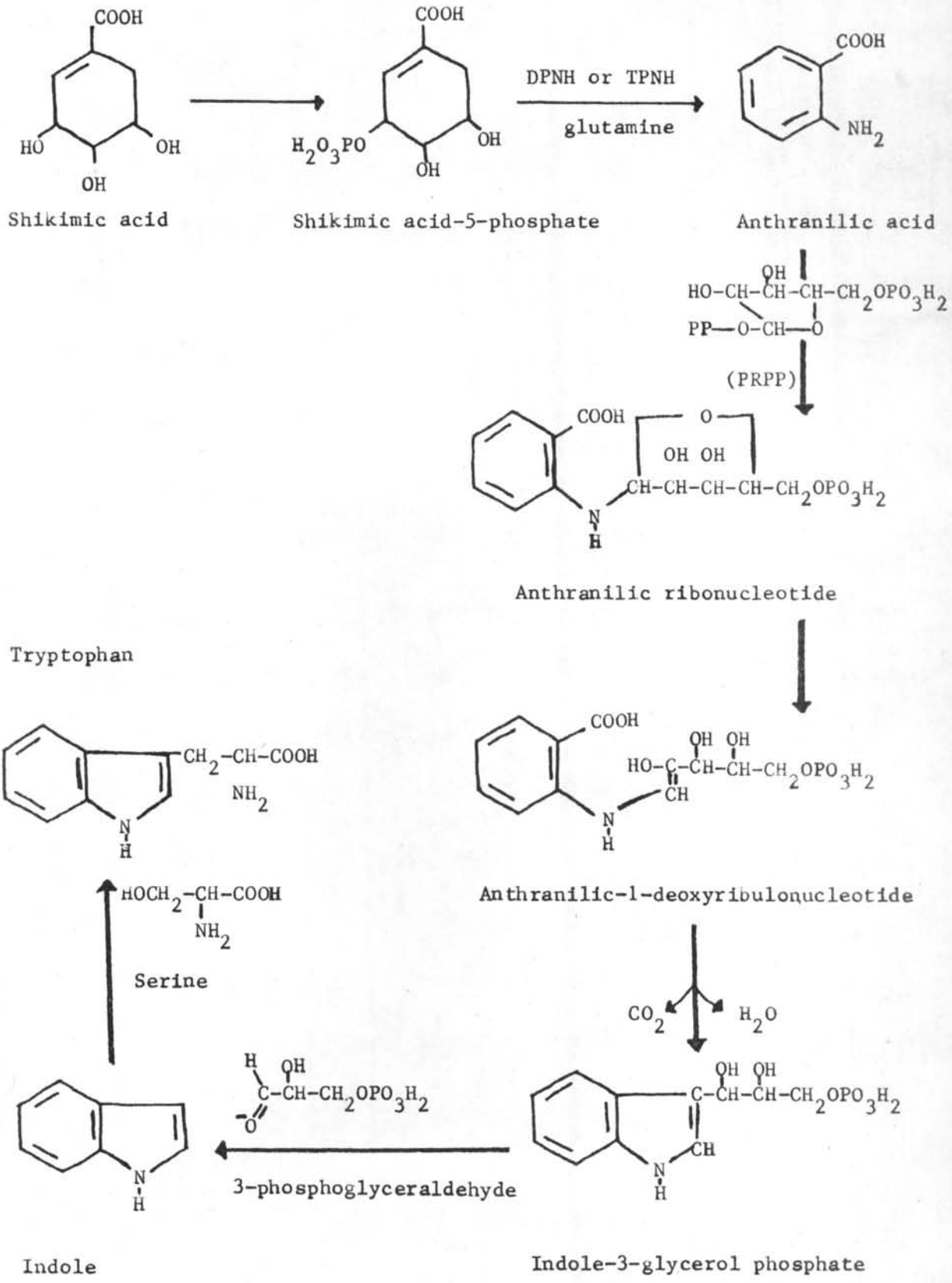
Indole Alkaloids

Biogenesis studies of indole alkaloids have shown that one of their precursors is tryptophan or its decarboxylate derivative, tryptamine. The other main precursor is called non-tryptophan derived unit.

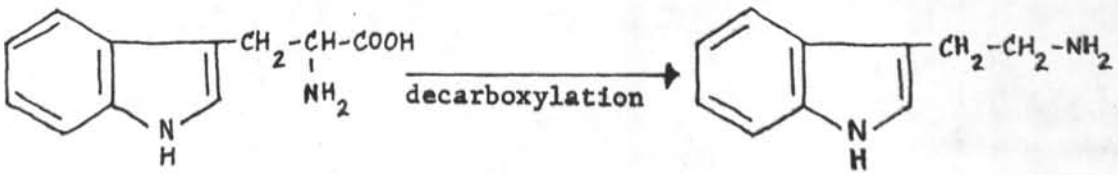
Formation of Tryptophan and Tryptamine

Tryptophan is derived from erythrose-4-phosphate and phosphoenolpyruvate via shikimic acid, anthranilic acid, indole-3-glycerol phosphate, indole and then combined with serine. More details are shown in the following scheme (Mattoon, 1963; Milborrow, 1973).




COOH
HO
OH
OH
Shikimic acid
COOH
H_2O_3PO
OH
OH
Shikimic acid-5-phosphate
DPNH or TPNH
glutamine
COOH
NH_2
Anthranilic acid
OH
$HO-CH-CH-CH-CH_2OPO_3H_2$
$PP-O-CH-O$
(PRPP)
COOH
O
OH OH
$CH-CH-CH-CH-CH_2OPO_3H_2$
N
H
Anthranilic ribonucleotide
Tryptophan
$CH_2-CH-COOH$
NH_2
N
H
COOH
OH OH
$HO-C-CH-CH-CH_2OPO_3H_2$
CH
N
H
Anthranilic-1-deoxyribulonucleotide
$HOCH_2-CH-COOH$
NH_2
Serine
CO_2
H_2O
H
OH
$C-CH-CH_2OPO_3H_2$
O
OH OH
$C-CH-CH-CH_2OPO_3H_2$
CH
N
H
3-phosphoglyceraldehyde
N
H
Indole
Indole-3-glycerol phosphate

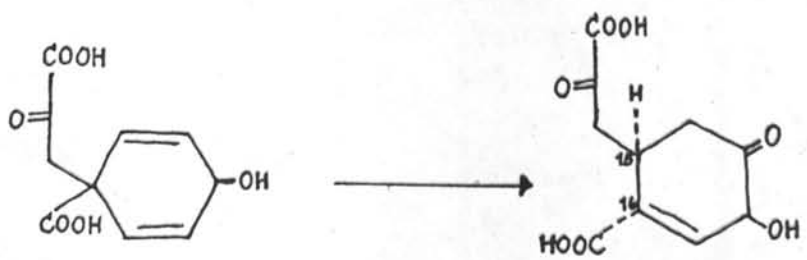
In some plants, indole alkaloids are not derived from tryptophan, but from tryptamine, its decarboxylate derivative.



Tryptophan Tryptamine

The non-tryptophan derived unit.

This unit is derived from a monoterpenoid moiety or C_9-C_{10}unit. Many scientists presented different hypotheses, e.g. Woodward, who indicated 3,4-dihydroxyphenylalanine to be the precursor but later Leete *et al.* in 1962 disproved it. Wenkert brought the other idea, the prephenic hypothesis, which suggested hydroaromatic compound or prephenic acid as the precursor of indole alkaloids. From this idea, the carboxylic group attachs to the C-16 and the hydrogen at C-15 of the yohimbine ring are shown to be of α-configuration.

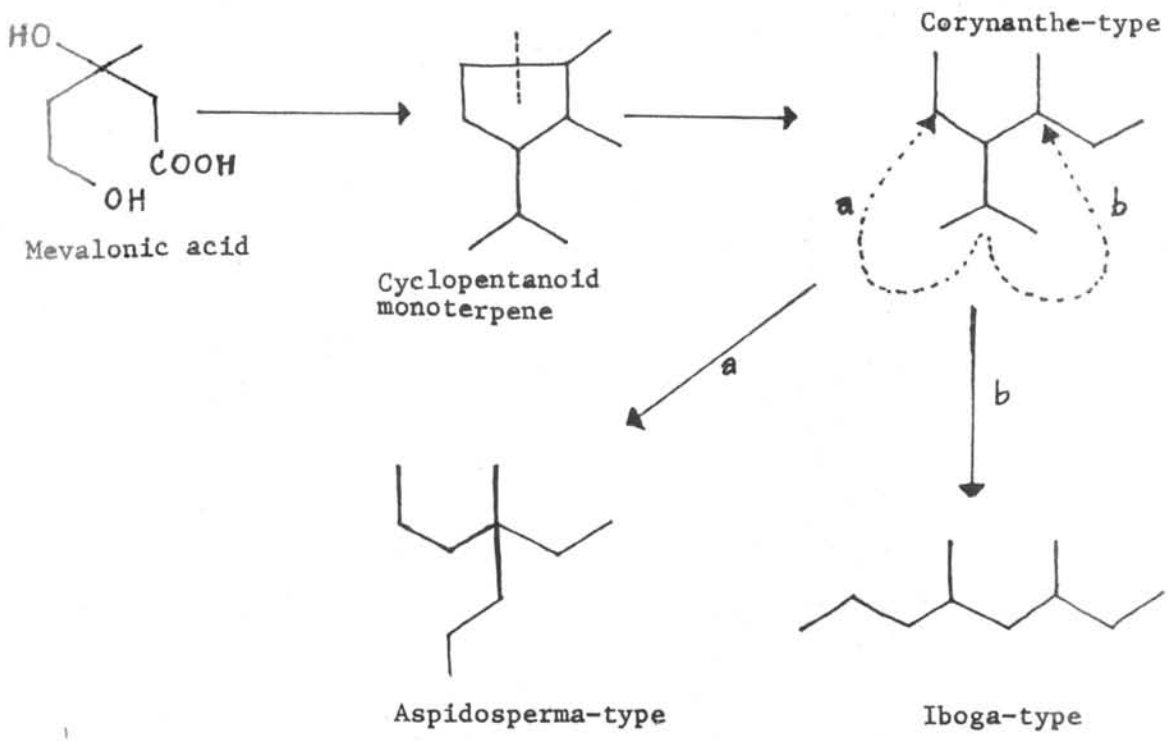


Prephenic acid

The experiments of Stoll and his coworkers in 1965 disagreed with the idea that prephenic acid was the precursor of C_9-C_{10}unit.

Acetate hypothesis explained the precursor to be three molecules of acetic acid condensing with one molecule of malonic acid and formaldehyde. Using radioactive techniques, this hypothesis was disproven (Leete *et al.*, 1965).

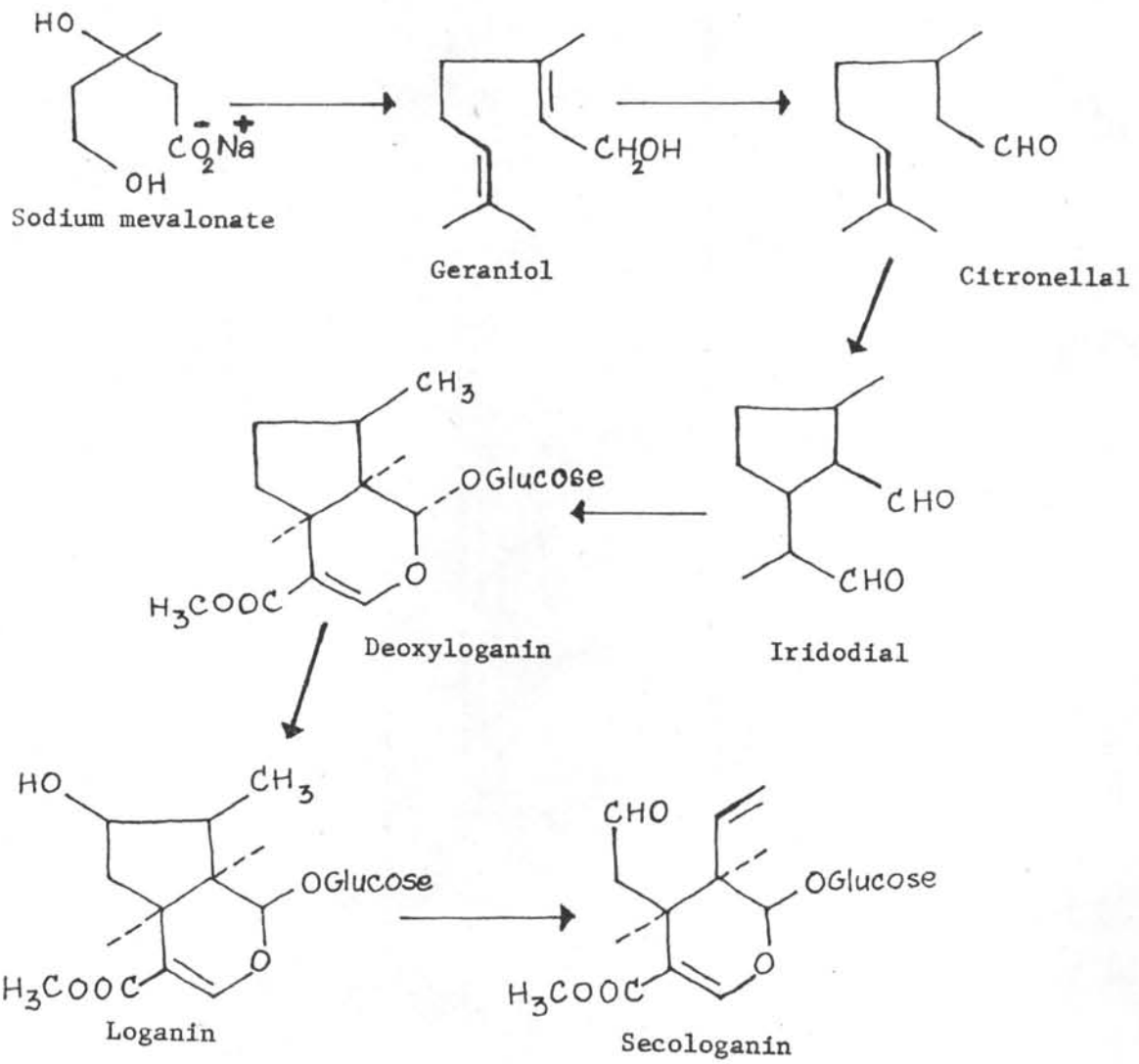
The only hypothesis accepted now is Thomas and Wenkert monoterpene hypothesis. Two molecules of mevalonic acid are responsible as the precursor, cyclopentanoid monoterpene as the intermediate, and then modified to the three major types of indole alkaloids, the corynanthe, the aspidosperma and the iboga-type.



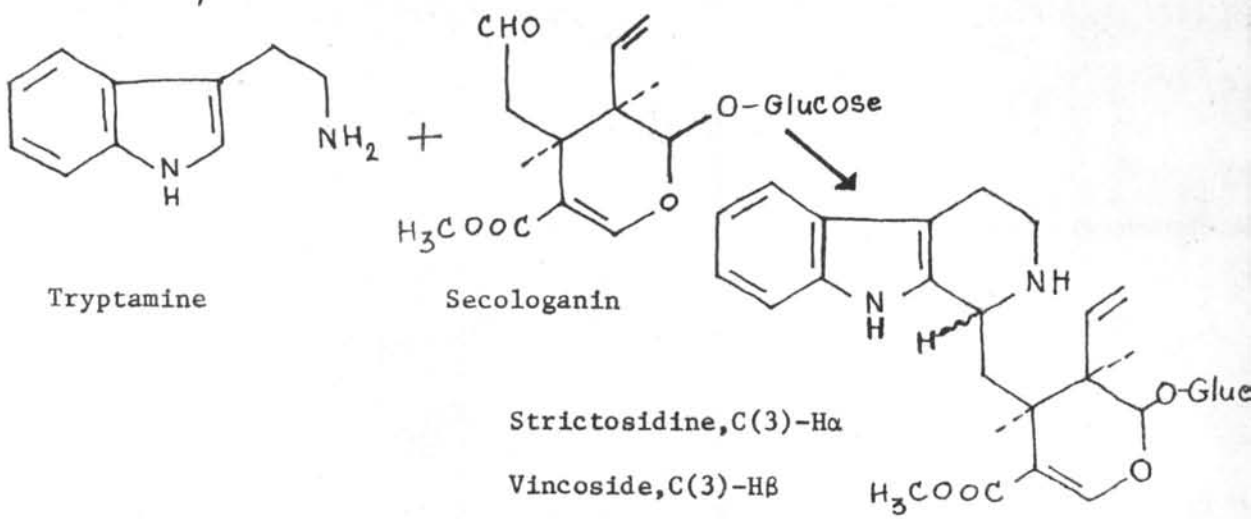
Labelled sodium mevalonate and geraniol were fed to *Catharanthus roseus* and catharanthine and dehydroaspidospermidine were detected. Degradation of these alkaloids gave results in agreement with head-to-tail combination of two C-5 units. Geraniol was then proved to be the precursor of indole alkaloids (Battersby *et al.*, 1966a,b).

Battersby and his coworkers (1966b) found that loganin was the most possible cyclopentanoid monoterpene intermediate in the biosynthesis of indole alkaloids while other cyclopentanoid monoterpene e.g. verbenalin, genepin, monotropeine methyl ester were negatively proved.

Battersby, in 1967, showed that the formation of loganin and secologanin from sodium mevalonate, via geraniol, citronellal and iridodial was as shown below.



Secologanin is the last intermediate of the non-tryptophan derived portion before it is condensed with tryptamine to generate vincoside and/or strictosidine(isovincoside) (Battersby,1968).

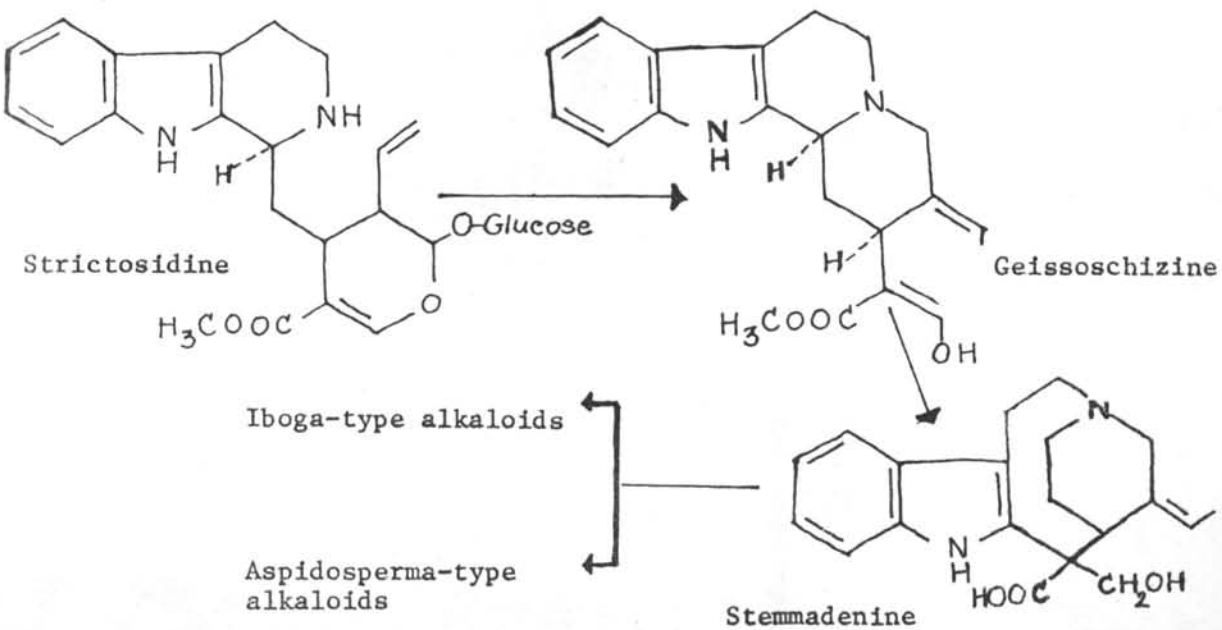


Tryptamine Secologanin

Strictosidine,C(3)-Hα

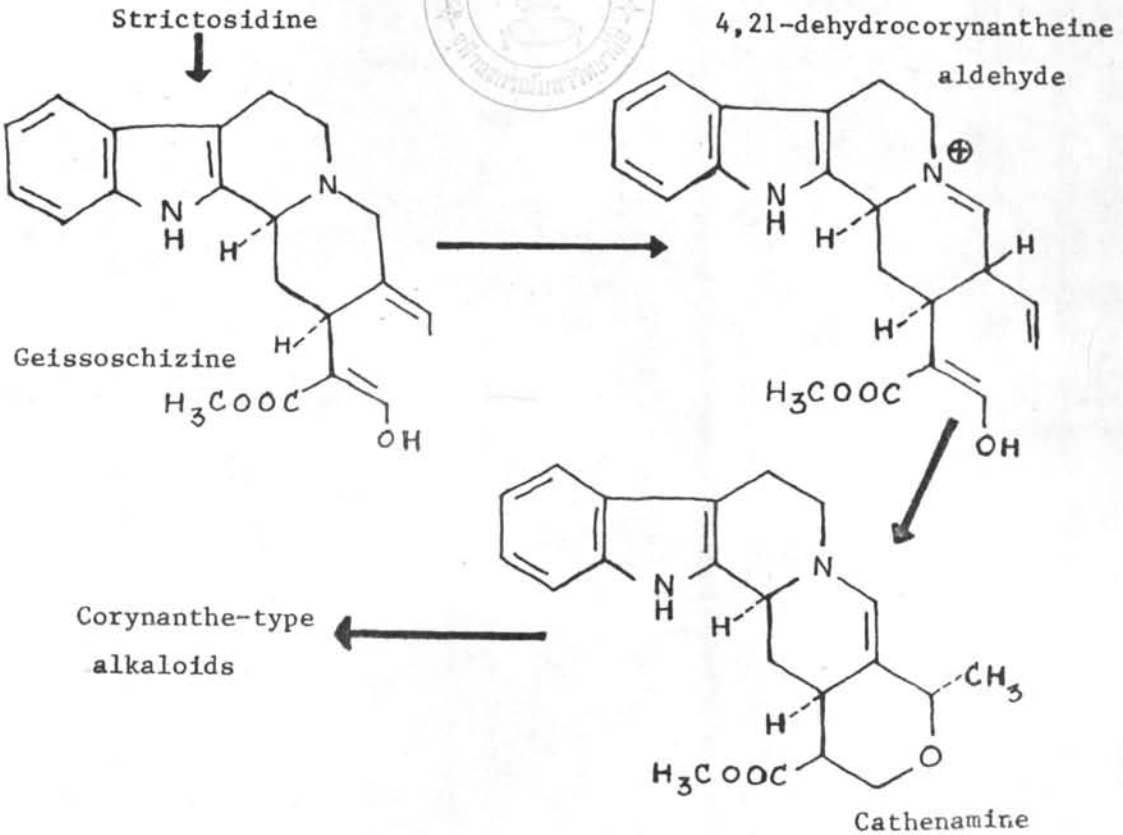
Vincoside,C(3)-Hβ

From a comparison of optical rotation differences between vincoside lactam and strictosamide, Blackstock *et al.* and De Silva *et al.* in 1971 determined the absolute configuration at C3-H in vincoside as β and strictosidine as α. Because of this, strictosidine,instead of vincoside, is served as universal intermediate in the biosynthesis of the three major types of indole alkaloids (Rueffer *et al.*,1978; Nagakura *et al.*, 1979).



Strictosidine Geissoschizine

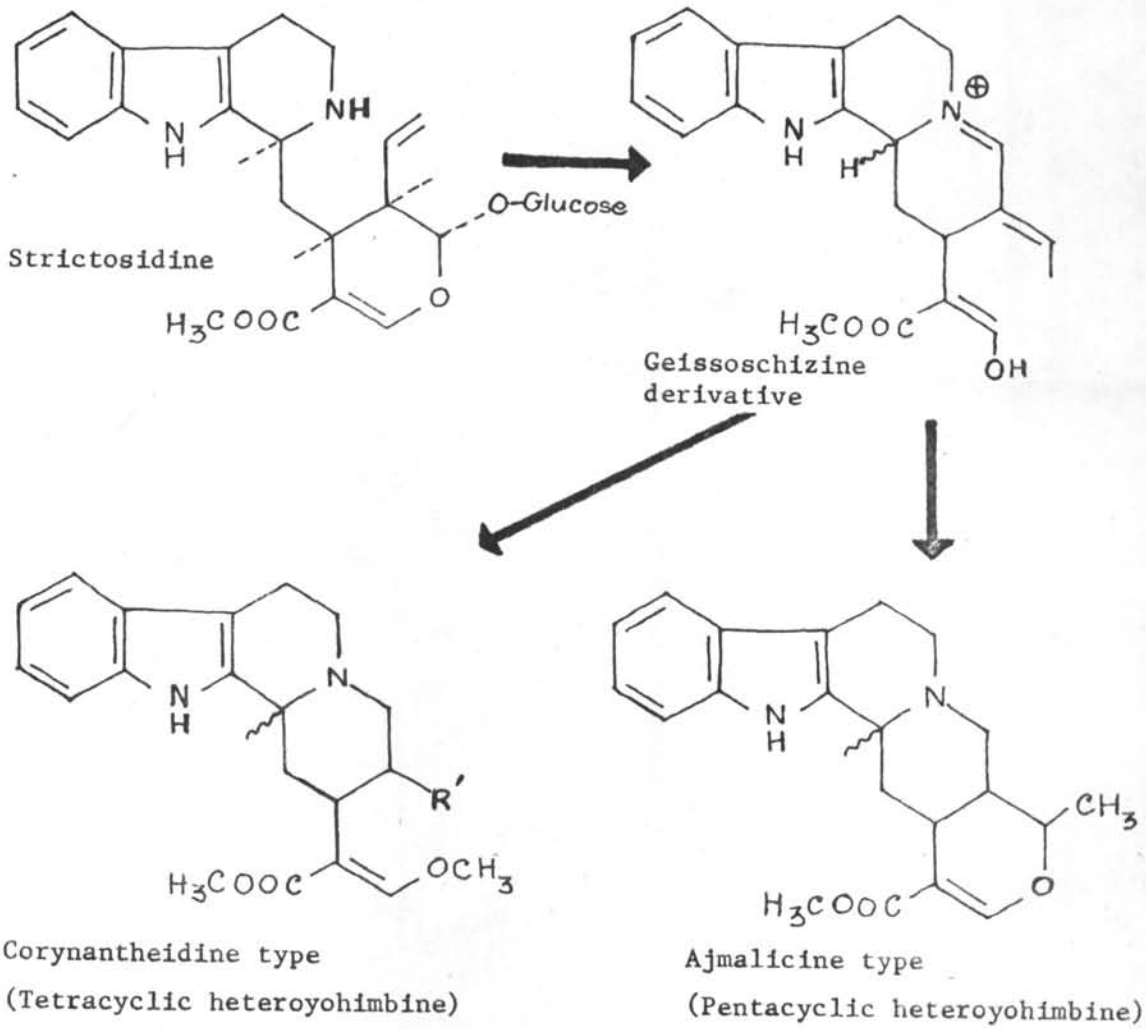
Stemmadenine



(Stokigt *et al.*, 1978; Heinstein *et al.*, 1979; Stockigt, 1979; Zenk, 1980)

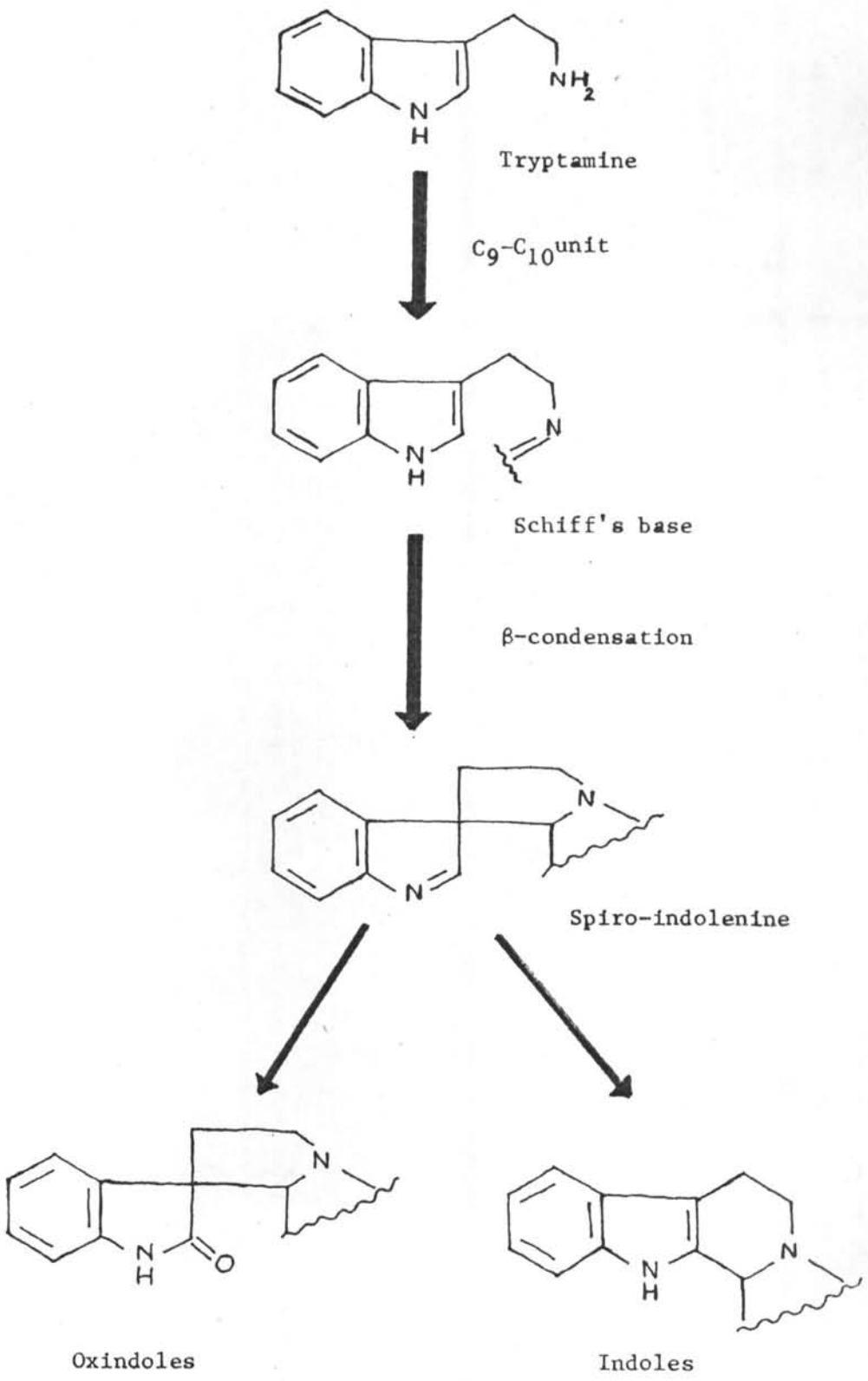
Geissoschizine is the further intermediate for corynanthe, aspidosperma and iboga-type indole alkaloids, the two latters have stemmadenine as the last intermediate.

The indole and oxindole alkaloids which were isolated from the genus *Uncaria* are corynanthe-type. The pentacyclic and tetracyclic heteroyohimbines are biosynthesised from strictosidine via geissoschizine derivatives as shown below:-



(Shellard *et al.*,1969b; Rungsiyakul,1973)

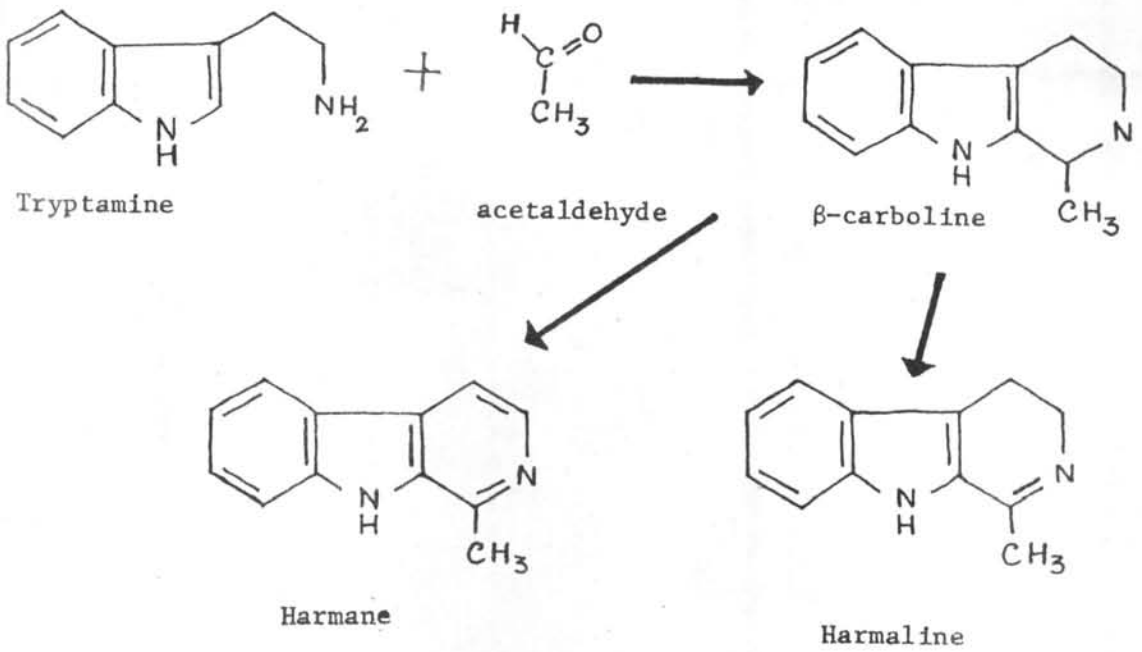
Oxindole alkaloids were derived by β-condensation from tryptamine and C_9-C_{10} unit (Woodward,1948). Jackson and Smith (1968) have arqued that the β-condensation is more favoured both to yield indole and oxindole alkaloids. The pathway is shown below.


NH2
N
H
Tryptamine
C9-C10 unit
N
N
H
Schiff's base
β-condensation
N
N
Spiro-indolenine
N
N
H
O
Oxindoles
N
N
H
Indoles

Formation of other indole alkaloids.

1. β-carbolines derivatives :- harmane, harmaline

These alkaloids are derived from the condensation of tryptamine and aldehyde, especially acetaldehyde (Robinson, 1968).

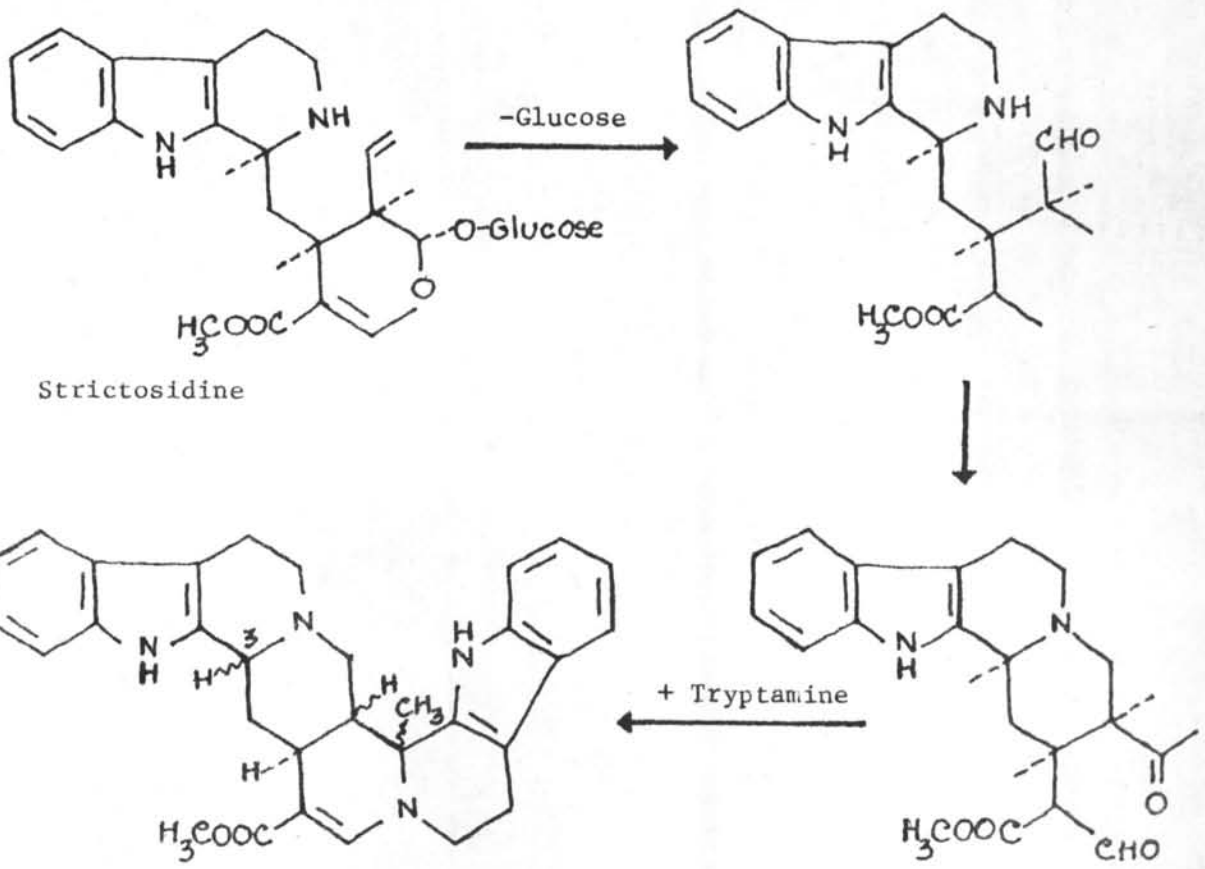


Tryptamine acetaldehyde β-carboline

Harmane Harmaline

2. Roxburghines

Battersby *et al.* (1968) and Merlini *et al.* (1970) proved the roxburghines to be derived from strictosidine and tryptamine. The possible biogenetic scheme is demonstrated as in the following :-

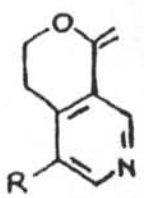


Strictosidine

Roxburghines

3. Pyridino-indolo-quinolizidinones.

Angustine and angustoline are derived from tryptamine and secologanin monoterpene unit closely related to the alkaloid gentianine.



Gentianine

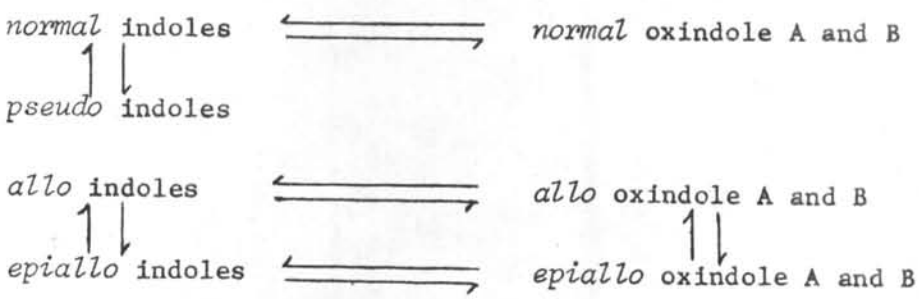
Battersby *et al.*, in 1969, suggested that angustine and angustoline might be formed from vincoside-lactam or strictosamide. The biogenesis of angustidine might involve the loss of a carbon atom C-21 from the secologanin portion of a corynanthe precursor (Au *et al.*, 1973).

Biogenesis of the *Uncaria* alkaloids.

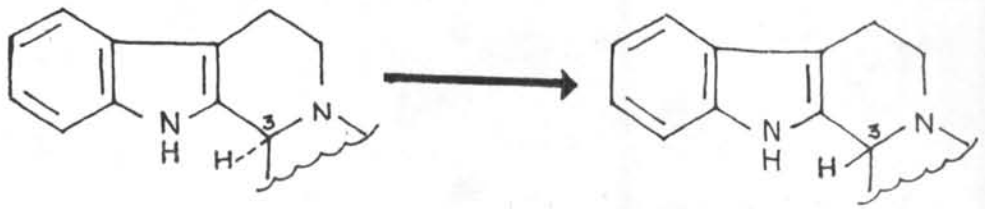
Shellard, Phillipson and Gupta (1969) observed that when and oxindole alkaloids occured in the same plant, the D/E ring systems were identical in both types and indoles were pressent in major quantities as their least stable configurations, *pseudo* and *epiallo*. They also postulated a hypothesis that the plant synthesised the more stable indole alkaloids and then isomerised to less stable isomers. Both indoles were converted to the corresponding oxindole alkaloids.

It should be noted that no *pseudo* oxindole alkaloids have been isolated naturally. Trager *et al.* (1968a) suggested that they were too unstable to exist but Brown and Platt (1976) succeeded in synthesising the *pseudo* oxindoles which were reasonably stable.

Jackson and Smith in 1968(a) suggested that the indole alkaloids also were formed from the oxindole alkaloids. These can be demonstrated briefly as follows.



In terms of configuration, the isomerisation of the indole alkaloids involves the conversion of C(3)-Hβ (Shellard and Houghton, 1973).

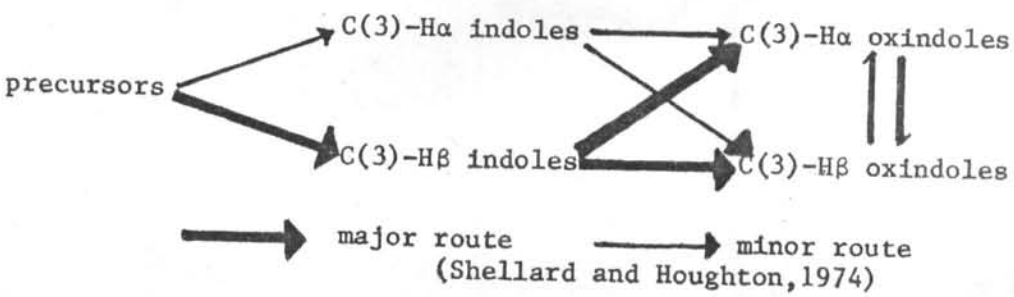


allo , *normal* *epiallo* , *pseudo*

There is no interconversion between *normal* and *pseudo*, and, *allo* and *epiallo* indole alkaloids during their biogenesis. By using ^{14}C-labelled indole alkaloids the C(3)-Hα and C(3)-Hβ alkaloids were also shown to be separately synthesised from the precursor. The *epiallo* and *pseudo* indoles were dominant and offered the main pathway to the oxindole alkaloids.

At that time, with the belief that the precursor, vincoside, possessed a C(3)-Hα, it was logical to expect that the plant would synthesise alkaloids with C(3)-Hα initially and isomerise into C(3)-Hβ alkaloids. Blackstock *et al.* and De Silva *et al.* in 1971, have shown that vincoside possesses C(3)-Hβ. Since *epiallo* and *pseudo* indole alkaloids are dominant, they can be converted into *allo* and *normal* oxindole alkaloids.

The minor biogenetic route would be existed whereby C(3)-Hα indoles are formed. The modified hypothesis may be shown as follows :



(Shellard and Houghton, 1974)

Shellard *et al.* (1978a) presented that if there is no evidence of interconversion between the substituted and non-substituted indole alkaloids, there are 8 possible biosynthetic routes for the alkaloids as were shown in the following table.

series	open E ring	closed E ring
normal-pseudo	1. C-9 H	5. C-9 H
	2. C-9 OCH_3	6. C-9 OCH_3
allo-epiallo	3. C-9 H	7. C-9 H
	4. C-9 OCH_3	8. C-9 OCH_3

Only unsubstituted indole alkaloids are reported from *Uncaria* species, i.e. series 1,3,5 and 7.

Stockigt and Zenk in 1977 proposed the role of isovincoside (C3-Hα) as a precursor in cell-free enzyme systems from *Catharanthus roseus* L. cell suspension cultures. The major route is via the C(3)-Hα indole alkaloids which are converted to C(3)-Hα oxindoles and to C(3)-Hβ indole alkaloids. The minor route is via the C(3)-Hβ indoles which are converted to the oxindoles. The scheme may be illustrated as follows :